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PRIMARY CARCINOMA OF THE LUNG*

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The present widespread interest and increasing attention devoted to primary carcinoma of the lung is thoroughly deserved. Any disease entity which rises from almost complete obscurity to one of the foremost subjects of the day in the relatively short period of a few decades demands serious consideration. At the beginning of this century primary carcinoma of the lung was considered a museum curiosity. At the present time it is one of the most frequent primary malignancies of the body. Such a phenomenal rise to prominence immediately presents an intriguing challenge to the zetetic medical mind. Of even greater practical importance is the problem of therapy. No longer than a decade ago the prognosis in this condition was considered absolutely hopeless. In that short span, as a result of the rapid strides that have been made in the technical developments of thoracic surgery, the prognosis has become relatively favorable. A number of cases have now been recorded in which the patient has lived five years or more after operation. Indeed, the technical developments of the thoracic surgeon have now evolved to such a perfected state that the most important responsibility depends upon early diagnosis. For these reasons, it is considered opportune to emphasize the practical significance of this disease, its early clinical manifestations, and the available methods of diagnosis and treatment.

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INCIDENCE

In 1912, Adler,[1] who reviewed a large series of collected cases of primary carcinoma of the lung, stated, "On one point, however, there is nearly complete consensus of opinion and that is that primary malignant neoplasms of the lung are among the rarest forms of the disease." At the present time such a statement would be actually ludicrous. However, it serves to show the rapid increase that has occurred in the incidence of this condition during the past few decades. Numerous authors[2-7] have recently presented studies which show that at present the *lung ranks second only to the stomach as the primary site of cancer*. That there has been a rapid and steady increase in the incidence of this condition is clearly demonstrated by numerous reports from individual institutions. In the Department of Pathology of the University of Leipzig, Assman[8] found that the incidence of carcinoma of the lung to all autopsies from 1900 to 1906 was 0.67 per cent and that of all the carcinomas, 5 per cent were pulmonary malignancies. From 1919 to 1922 these corresponding figures had increased to 1.54 and 9.17 per cent. Similarly, Holzer[9] observed that from 1895 to 1904 the percentage of carcinoma of the lung to all carcinomas was 1.04 per cent. Whereas there was no rise in the incidence of total cancer, there was a steady increase in the incidence

of pulmonary malignancies. Thus, from 1915 to 1924 these corresponding figures were 0.47 per cent and 6.69 per cent. At the Dresden City Hospital, during the 67-year period, 1852 to 1919, the incidence of carcinoma of the lung as based upon all malignancies in postmortem examinations increased fivefold.[10-12] At the London Hospital, Simpson[13] found that there was a steady increase in the incidence of lung cancer in necropsies from 0.51 per cent in 1907 to 2.05 per cent in 1925. Duguid[14] also found a somewhat similar rise in the incidence of intra-thoracic malignancies at the Manchester Royal Infirmary. Probst[15] reviewed the incidence of lung cancer in postmortem cases in Zurich from 1906 to 1926 and found that whereas the incidence of cancer to all autopsies increased only from 10 per cent to 13.1 per cent, the incidence of pulmonary malignancies to all carcinomas increased from 0.19 per cent to 0.99 per cent. Huguenin,[16] in France, and Piayd[17] in Russia, also concluded that there has been a real increase in this condition in their respective countries. Lóizaga[18] in Buenos Aires, reported an incidence of 5.18 per cent of lung cancer in all postmortem carcinomas during the period 1898 to 1917, and this increased to 14.6 per cent during the years, 1918 to 1937.

Similarly, in this country, numerous authors from various sections have found a definite increase in the incidence of this disease. Thus, Weller,[19] at the University of Michigan Hospital, observed that the incidence of carcinoma of the lung in the first 1000 autopsies was 0.1 per cent, in the second 0.5 per cent, and of 450 in the third, 0.8 per cent. At the University of Minnesota, Barron[20] found that the incidence of lung cancer in the autopsy cases during 1899 to 1911 was zero, during 1919 to 1918, 0.19 per cent, and during 1919 to 1921, 0.89 per cent. Olson[21] reviewed the cases at the Boston City Hospital and found that the incidence of pulmonary carcinoma to all carcinoma increased annually from 7.5 per cent in 1929 to 19.1 per cent in 1934. In the autopsies performed at the Veteran's Bureau Hospital, Matz[22] observed that during the period, 1927 to 1931, the incidence of carcinoma of the lung to all carcinoma was 6.4 per cent and during the years 1932 to 1937 it was 15.8 per cent. Based upon an analysis of a collected series of cases Rosahn[23] found that the incidence of carcinoma in all autopsies increased from 10.27 per cent in the period 1910 to 1919, to only 12 per cent in the period, 1920 to 1928, whereas the incidence of carcinoma of the lung to all postmortems increased from 0.44 per cent to 0.89 per cent in these respective periods. At the Charity Hospital in New Orleans, during the past seven years, there has been an approximate fivefold increase in the incidence of necropsied pulmonary carcinoma.[5] Of even greater significance is the fact that during this same period the incidence of carcinoma of the stomach in necropsy cases has not increased. In a previous publication[6] we reviewed the mortality statistics in the United States of all persons dying of pulmonary malignancies during the period, 1920 to 1936 inclusive, and found that there was not only an actual increase in the number of deaths from this cause but also an annual increase in the death rate per hundred thousand population. Moreover, it was found that of the death rates of persons dying of malignancies of various organs the increase in the incidence of carcinoma of the lung was relatively greater.

It is obvious, therefore, from these statistics reported from various parts of the world, that the incidence of carcinoma of the lung is definitely and steadily increasing. In our opinion this increase is not only apparent but real. Whereas there is no definite explanation for this increasing incidence, numerous theories have been suggested. No attempt will be made here to review these in detail as they have been previously considered.[6] Based upon the increasing incidence of bronchiogenic carcinoma following influenza epidemics and upon the presence of metaplasia in bronchial mucosa in persons dying from this disease some have suggested a possible relationship between these conditions.[24-27] Other chronic specific and non-specific pulmonary infections such as tuberculosis,[28] syphilis,[13, 29] bronchiectasis,[30, 31] have also been consid-

ered. It is believed by some investigators that the inhalation of irritating gases such as war gas, exhaust gas of combustion motors, and gases arising from tarred roads, plays an etiologic role.[32-36] The high incidence of carcinoma of the lung among workers in the Schneeberg and Joachimsthal mines has long been known. On the basis of intensive studies made of these mines, it is believed that these malignancies are due to radio-active emanations.[37-39] Careful attention has been directed toward the possible etiologic significance of pneumoconiosis and silicosis in bronchiogenic carcinoma. Whereas some[40-42] contended that this may be a factor, others,[43, 44] are of the opinion that it is of little significance unless the inhaled dust contains carcinogenic substances. The probable significance between the increase in smoking and the increase in pulmonary malignancy has been previously emphasized by the authors.[6, 7, 45] Numerous investigators have repeatedly demonstrated the irritating carcinogenic effects of tobacco.[46-50] Roffo,[51] on the basis of his extensive investigations, is convinced that tobacco is one of the most important carcinogenic agents. He has been able to produce tumors in rabbits as easily with tobacco tar as with coal tar. Hoffmann[52] is "strongly of the opinion that a relation between the increase in smoking habits and cancer of the lung may be safely assumed to exist." We[6] found a significant relationship between the increased incidence of carcinoma of the lung in the United States and the increased production of tobacco.

The sex incidence of primary carcinoma of the lung reveals a preponderance in the male. Simons[53] reported that males predominated in a ratio of four to one. In a collected series of 8,575 cases, it was found that 78.9 per cent were males and 21 per cent were females.[3] The effect upon the sex incidence of the recent increase in women smokers will be interesting to observe.

Carcinoma of the lung occurs with greatest frequency in the fifth and sixth decades. In Brunn's[54] series, 62 per cent occurred in this age group. Breckwoldt[55] found the most frequent occurrence between 50 and 70 years. Fischer[56] observed that one-third occurred in the fifth decade and one-third after the age of 60. In a series of 4,307 collected cases we[6] found that approximately 60 per cent occurred between the ages of 40 and 60 years and about 80 per cent between the ages of 40 and 70 years. It was significant, however, that 10.7 per cent occurred between the ages of 30 and 40 years. Weill[57] reported a case in a child one year of age and Frommel[31] in a patient 91 years of age.

PATHOLOGY

In the past it was believed that some lung cancers were alveolar in origin, but at present it is the consensus that practically all primary carcinomas of the lung are bronchiogenic and originate from the basement cells of the bronchial or bronchiolar mucosa. Because of the characteristic pleomorphism of these neoplasia considerable variation in the histopathologic classification has resulted. The majority of observers have classified them into three general groups: (1) Squamous cell carcinoma, (2) small or undifferentiated cell carcinoma (oat cell), and (3) adenocarcinoma. We are of the opinion, however, that the most logical classification is that proposed by Halpert[58] and based upon the development of the cells lining the bronchi. The cells of the mucous membrane lining the bronchi and bronchioles normally represent varying degrees of differentiation and specialization of the original entodermal cells. According to Halpert[58] the undifferentiated entodermal ancestor cell is capable of developing into a variety of cells including the ciliated cylindrical and goblet cells. Beneath these and lined up along the border of the tunica propria are the cells from which the ciliated cylindrical and goblet cells are replenished and which he calls "reserve cells." In his opinion carcinoma of the lung originates from these "reserve" cells by atypical proliferation. On this basis and depending upon the type of cell which predominates primary carcinoma of the lung may be classified into three groups: (1) Reserve cell carcinoma, (2) cylindrical cell carcinoma, and (3) squamous cell carcinoma.

These neoplasia occur most frequently in the hilar region. Boyd[59] found that 90 per cent were centrally located and Edwards[60] states that only 20 per cent are peripheral. Others[4, 19] have also observed that only a small incidence, less than 15 per cent, were peripheral. Depending upon the site of origin the gross changes will vary. The more centrally located tumors eventually produce bronchial obstruction with consequent atelectasis distally and secondary infection. The peripherally located tumors are more circumscribed solid masses of tissue which later show central necrosis.

The right side has been found to be involved more frequently than the left. Fischer[56] collected a series of 3,735 cases and found the right side involved in 53 per cent, the left in 45, and the lesion bilateral in 2 per cent. The right upper lobe bronchus was most frequently involved and in the order named the next most frequent were: The right main bronchus, the left upper lobe bronchus, the right lower lobe bronchus, the left main bronchus, and the left lower lobe bronchus. In a collected series of 4,732 cases we[6] found the right lung involved in 58.3 per cent and the left in 41.6 per cent.

Metastasis from primary carcinoma of the lung occurs by direct extension, through the lymphatics, by way of the blood stream, and by "bronchial embolism." The most frequent sites of metastatic involvement are the regional lymph nodes, and the next most frequent is the liver. Olson[21] found the tracheobronchial lymph nodes involved in 86 per cent and the liver in 35.8 per cent. Frissell and Knox[61] found extension to the regional lymph nodes in 97.4 per cent. In the collected series analysed by Miller and Jones[62] the liver was involved in 30.7 per cent. In a series of 2,579 cases collected by us[6] the regional nodes were involved in 75.9 per cent, the liver in 33.4 per cent, the bones in 20.4 per cent, the adrenals in 17.6 per cent, the kidneys in 16 per cent, the brain in 14.6 per cent, the heart and pericardium in 10.4 per cent, and the pancreas in 5.1 per cent.

CLINICAL MANIFESTATIONS

The authors have previously emphasized the fact that there is no characteristic clinical picture of primary carcinoma of the lung. When the condition has progressed to the stage in which the clinical manifestation obviously reflects the diagnosis, the prognosis is hopeless. It is imperative, therefore, to consider the earlier manifestations. The onset is characteristically so insidious that frequently it is difficult to determine just when the symptoms began. This is particularly true of smokers, because they almost invariably complain of a chronic cough and cough is not only the most constant but also one of the earliest symptoms of carcinoma of the lung. It is indeed unfortunate that the almost universal use of tobacco has resulted in a habitual cough, because the complaint of cough in the patient with an early carcinoma of the lung is likely to be disregarded and attributed to smoking. Usually the cough is nonproductive in the early stages but later is accompanied by expectoration which becomes progressively more profuse and mucopurulent in character and frequently blood tinged.

In our experience the patient frequently dates the onset of his illness to a recent acute respiratory tract infection, such as an acute bronchitis or influenza. Following this acute illness he continues to have thoracic involvement and in spite of treatment does not seem to improve.

Hemoptysis is not a frequent manifestation in the early stage. Brines and Kenning[3] found that hemoptysis was the chief complaint in 18.9 per cent of their series but was present some time during the course of the illness in 48.3 per cent. Simons[53] observed that it occurred in 40 per cent of his collected series. In elderly patients hemoptysis is particularly significant, as it always suggests the possibility of carcinoma of the lung. Thoracic pain is a variable complaint and is frequently an early manifestation. However, its vague and indefinite character is likely to cause it to be disregarded by the patient. Brines and Kenning[3] found it present in 60 per

cent of their series and the chief complaint in 44.8 per cent. Frissell and Knox[61] and Simons[53] found that it occurred in approximately 72 and 60 per cent of their respective series. In the more peripherally located tumors, pain is frequently the earliest symptom. Characteristically, this pain persists in spite of therapy. Dyspnea, pyrexia, emaciation, and weakness are obviously late manifestations.

The duration of symptoms varies considerably, but in the reported statistics the period of time elapsing between the onset of symptoms and death is relatively short. Koletsky[4] found that the average duration of symptoms from onset until death was about six months. King[63] reported an average duration of life of 9.3 months. In the Charity Hospital series[5] this period was five months. Whereas from these statistics it would appear that carcinoma of the lung is a rapidly progressive condition, it is our opinion that these reports do not necessarily indicate the true duration of symptoms. As previously emphasized[6] these figures are based upon autopsy cases, and consequently, no serious effort may have been made to elicit inaugural symptoms. In one of the authors' cases hemoptysis was the first manifestation noticed and occurred two weeks before admission, although the patient, who was a heavy smoker, had had a cough for a period of years. At operation a relatively large tumor, involving the hilar region and consequently inoperable, was found. The authors have had several other cases in which the lesion obviously had been present for a long period of time, although according to the history the duration of symptoms was relatively short.

The physical findings in primary carcinoma of the lung are extremely variable and depend upon the type and extent of the lesion as well as the location. Not infrequently there are absolutely no abnormalities upon physical examination. This occurs especially in the earlier stages. Later limitation of expansion, dulness, decreased breath sounds, and rales may be present. Unfortunately, such obvious physical signs are generally indicative of inoperability.

DIAGNOSIS

As previously stated, the most important factor in the diagnosis of primary carcinoma of the lung is the consideration of its possible presence. Every patient forty years of age or older who complains of cough, hemoptysis, or thoracic discomfort should be suspected of having pulmonary carcinoma until this diagnosis has been absolutely excluded. Careful roentgenographic studies should always be made. In the early stages the roentgenographic interpretation of centrally located lesions which are the most frequent type is generally more difficult because of confusion with hilar shadows produced by other lesions and by normal structures. As the lesion progresses, bronchial obstruction eventually occurs with consequent atelectasis of one or more lobes. The roentgenogram then reveals a shadow with displacement of the mediastinal structures toward the affected side. In the peripherally located tumor the roentgenographic shadow is more clearly defined and may be differentiated earlier. That roentgenographic examination is an important procedure is clearly demonstrated by the high incidence of correct diagnoses reported following its use. Andrus[64] and Vinson[65] have reported correct diagnoses by roentgenographic examination in over 90 per cent of the cases.

Because of the fact that the great majority of these lesions are centrally located, bronchoscopy may be considered one of the most important diagnostic procedures in primary bronchiogenic carcinoma. The bronchoscopic visualization of the tumor and the removal of a section for biopsy study obviously increase the accuracy of diagnosis. However, in those cases in which the lesion involves the upper lobe bronchi difficulty may be encountered in demonstrating the tumor. Recently, Gebauer[66] has reported a bronchoscopic mirror which he devised for upper lobe visualization. The incidence of positive diagnoses by means of bronchoscopy is over 70 per cent. A number of authors have described the characteristic bronchoscopic features and no attempt will be made here to discuss them in detail.[67-71]

Bronchography is another important diagnostic procedure and is particularly advantageous in those cases in which the tumor mass does not cast a shadow. Intratracheal instillation of lipiodol followed by roentgenographic examination may reveal partial or complete occlusion of the bronchi. Not infrequently bronchial narrowing is tapering in character. The transglottic method previously described for the instillation of lipiodol is considered one of the simplest.[72]

Aspiration biopsy is another diagnostic procedure which has been suggested. This procedure has the advantage of permitting the accurate demonstration of malignancy especially in peripheral lesions but, as previously emphasized, is dangerous because of the possibility of transplanting malignant cells into the tissues through which the needle passes. The demonstration of malignant cells in expectorated material was early described by Dudgeon,[73, 74] who was able to make a diagnosis in 60 per cent of the patients by this procedure. It is important, however, that a pathologist trained in this technic and in the recognition of these cells perform the examination. Similarly, examination of aspirated pleural fluid may also reveal the presence of malignant cells. This procedure was described by Mandlebaum,[75] and Seecof[76] and Goldman[77] reported incidences of positive diagnoses in 70 and 80 per cent respectively. Usually, however, when the diagnosis can be made by this method, the tumor is inoperable.

TREATMENT

It is a generally accepted fact that the only curative treatment of carcinoma of the lung is surgical extirpation. Radiation therapy has failed miserably in the treatment of primary carcinoma of the lung. This procedure has been employed in alleviating the manifestations and has been reported to prolong life for possibly a few months, although this is also doubtful.[78] Maxwell and Nicholson[79] found that roentgen therapy may have prolonged life in four of sixteen cases and in three it undoubtedly caused a more rapid fatal termination. Others[80-82] have reported somewhat similar experiences.

A number of authors have reported the procedure of simple lobectomy of the involved lobe in the surgical treatment of primary carcinoma of the lung, but it is now the consensus among thoracic surgeons that pneumonectomy is the only rational procedure. Only by its performance can the regional lymph nodes, which as previously shown are involved in a relatively high incidence of cases, be extirpated together with the primary lesion. In a previous publication[45] we described in detail the technic of the operative procedure, and for this reason no attempt will be made here to discuss it at length. In general, two approaches may be employed, either an anterior or a posterolateral. After entering the pleural cavity and freeing all adhesions, the hilar structures are exposed by incising and mobilizing the mediastinal pleura. The hilar vessels are isolated individually and divided between transfixation ligation sutures of silk. The bronchus is severed between clamps and the stump closed by mattress sutures of silk. The mediastinal nodes are carefully extirpated. It is for this reason that individual isolation of the hilar structures should be done. Mass ligation does not permit removal of these glands. Pleuralization of the stump of the hilar structures is performed by approximating the anterior and posterior mediastinal flaps. The pleural cavity is closed without drainage.

The first pneumonectomy for carcinoma of the lung was probably performed by Kummel,[83] in 1910. However, this patient died on the sixth postoperative day. Subsequently several other unsuccessful attempts were made but the first operation which recovered was performed by Graham[84] in 1933. This patient, a practicing physician, is still living and enjoying good health. Since then, a number of successful cases have been reported and the constantly increasing number of these cases is more and more encouraging.

We have previously analyzed a series of 101 cases collected from the literature and

15 personal cases. The mortality in the collected series was approximately 60 per cent and in our series, 53 per cent. Since this report we have performed four additional operations, giving a total of 19 and a mortality of 47.3 per cent. The causes of death in the collected series following operation were infection and pneumonia in 39.2 per cent, cardiac failure and pulmonary edema in 23.5 per cent, hemorrhage in 13.7 per cent, metastases in 9.8 per cent, thrombosis and embolism in 7.8 per cent, and shock, peritonitis and asphyxia in 1.9 per cent each.

SUMMARY

1. The incidence of primary carcinoma of the lung is definitely and steadily increasing. At present, the lung ranks second only to the stomach as the primary site of cancer. The various theories that have been advanced in an attempt to explain this increasing incidence are briefly reviewed.

2. Primary carcinoma of the lung occurs predominantly in the male sex. Its most frequent incidence is in the fifth and sixth decades.

3. There is no characteristic clinical picture of early carcinoma of the lung. The condition should be suspected in every patient past forty years of age who complains of cough that cannot be reasonably explained and that does not readily respond to appropriate therapy.

4. The pathologic features of the disease are discussed.

5. The available methods of diagnosis are reviewed and critically evaluated. Roentgenography and bronchoscopy are valuable diagnostic procedures and will provide an accurate diagnosis in over 70 per cent of the cases.

6. Radiation therapy is of little or no value in the treatment of primary carcinoma of the lung.

7. The only curative treatment is surgical extirpation of the involved lung. The results of operation are briefly reviewed.

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DISCUSSION

Dr. W. R. Mathews (Shreveport): Drs. Ochsner and DeBakey have quite properly emphasized the high incidence of carcinoma of the lung. As late as twenty years ago leading medical centers were reluctant to admit there were many cases of primary carcinoma originating in the lung. As a contrast today many hold that carcinoma of the lung is one of the most prevalent diseases. On the basis of autopsy and clinical observations and experience at large, indicated by Drs. Ochsner and DeBakey, from 10 to 15 per cent of all malignancies originate in the lung.

Dr. Julius Lane Wilson (New Orleans): There can be no question about the increasing incidence of pulmonary carcinoma. The Metropolitan Life Insurance Company, in a statistical bulletin a few months ago, showed that the mortality rate among policy holders has gone up in twenty years from 2.6 per hundred thousand to 15 per hundred thousand, between the ages of 45 and 74. These figures are interesting in connection with etiology. This

increase is divided according to sex and the interesting part of this graph, of which I have no slide, is that most of this increase, particularly since 1925, has been in the male sex, which they interpret to mean that tobacco has no particular influence because since 1918 there has been more increase in the use of tobacco by women.

As to symptoms, cough is rightly emphasized. Many smokers have chronic cough and many nonsmokers also cough in the morning. Perhaps we can say the important thing is a change of cough habit. These cases give a history of having developed a disturbing cough at all hours. An habitual cough is often not noticed by the person who has it. Pain, of course, is important although occurring in a much smaller percentage than cough. The characteristic pain is persistent and not relieved with ordinary measures,—strapping, fluid accumulation and aspiration do not change it. Hemoptysis, in the patients in whom it occurs, is an important symptom.

The physical signs, when well developed, are those of tumor or atelectasis.

I want to emphasize again Drs. Ochsner's and DeBakey's point about considering every man over 45 who has a cough not otherwise explained and particularly if there is blood in sputum, as a possible case of carcinoma of the lung.

I might also say a word about tuberculosis at this point. Somebody said that hemoptysis occurring in a person under 45 means tuberculosis and over 45 years of age, carcinoma. Tuberculosis can be ruled out by a chest x-ray and sputum examination. A male who has a persistent cough with or without hemoptysis and has not tuberculosis should be bronchoscoped because he very possibly has carcinoma of the lung.

Dr. P. R. Gilmer (Shreveport): I would like to emphasize a few points already brought out. In the first place early diagnosis of carcinoma of the lung naturally means a better opportunity for surgical removal and for permanent cure. That is accepted now and there is no doubt about it. From the diagnostic standpoint, I agree with Drs. Ochsner and DeBakey and certainly want to agree with Dr. Wilson's discussion. If we are going to diagnose carcinoma in an operable stage, it must be suspected first, just as, for instance, in the diagnosis of early tuberculosis. Most of those early cases are diagnosed first as "suspected carcinoma" and are then studied carefully and the final diagnosis made. If physicians keep carcinoma of the lung in mind and suspect it and remember, as Drs. Ochsner and DeBakey pointed out, and unexplained persistent cough is suggestive of carcinoma, these cases may be diagnosed sufficiently early.

Another point is that a negative radiograph of the chest does not, by any means, exclude carcinoma of the lung. As a matter of fact maybe we should not use the radiograph because we can not always see anything in the lung, especially in early cases. I think that brings us down to the point that if we suspect carcinoma of the lung the diagnosis is made and confirmed and proved only by bronchoscopic examination and biopsy. Obviously some of the upper lobe involvements are not going to be successfully biopsied but only a small percentage of cases occur in the upper lobe. In the lower lobe certainly bronchoscopy and biopsy can bring out correct diagnosis.

As to operability of patients, this depends upon the location of the primary growth. Obviously if high up and well infiltrated, there is no opportunity to remove it because there is no intervening healthy tissue at the hilus stump for suturing.

I would like to leave this thought. Suspect carcinoma of the lung just like you have been told to suspect early tuberculosis. Once suspected, do not stop there and even if there is a negative radiograph, have the patient bronchoscoped.

Dr. J. Ralph Phillips (Baton Rouge): How can you tell the difference between bronchiogenic carcinoma and aneurysm of the aorta? Sometimes it is very difficult to make a differential diagnosis between a bronchiogenic carcinoma and aneurysm of the aorta. I can remember one case in which the diagnosis had been made from x-ray and physical findings of a bronchiogenic carcinoma of the left bronchus, and on bronchoscopy a piece was taken from the tumor mass and on autopsy this mass turned out to be a aneurysm of the aorta which had eroded the left bronchus. Another case which I have in mind was diagnosed by x-ray and physical findings as a carcinoma of the right bronchus, and on bronchoscopy a non-pulsating mass was noted in the right bronchus. A biopsy was taken and again on autopsy an aneurysm of the aorta was found which had eroded the right bronchus. With these and other findings I have found it difficult at times to differentiate between an aortic aneurysm and carcinoma lung.

Dr. Ochsner (In closing): Unquestionably the diagnosis is difficult. It is bronchoscopically difficult. Only 75 per cent can be so diagnosed. We would rather depend upon exploratory thoracotomy. Recently we have seen a patient in whom the radiologist made a diagnosis of aneurysm. The patient's symptoms had progressed relatively rapidly which made us think he had a malignancy, which was verified by exploration. We would rather explore these individuals, and this is a point I would like to emphasize. At one time we felt that one was not justified in doing a thoracotomy unless the case was positively diagnosed tumor or by biopsy. That is not so now.

We felt that 19 of our patients had carcinoma of the lung. These patients were operated upon and a pneumonectomy done. Of our 19 patients in whom we were able to do a pneumonectomy for malignancy, ten of them left the hospital, two of them died on the table, and seven died in a period of convalescence in the hospital. Of the ten who left the hospital, eight are still living.

THE TREATMENT OF CHRONIC INFECTIOUS ARTHRITIS*

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The treatment of chronic infectious arthritis is one of the most difficult problems in internal medicine. As regards the treatment of the disease, physicians tend to group themselves roughly into three main groups. Physicians in the first group believe that treatment is entirely unsuccessful and that an individual contracting the disease is doomed to invalidism and hopeless crippledom. Fortunately for the patient, physicians in this group are relatively few. The second group constitutes the vast majority of physicians that the chronic arthritic patient consults. These physicians are bewildered by the claims and counterclaims of the various pharmaceutical manufacturers. The products recommended by these firms are found to be of value in occasional cases but in the majority of cases fail to produce the desired results. As a group, after repeated failures of highly touted therapeutic regimens, they rapidly drift into group one and become therapeutic nihilists. The third group is composed of physicians who have had a vast amount of experience in the treatment of rheumatism. They have seen many highly recommended remedies come and go and have come to the inescapable conclusion that there is no single remedial agent, either drug or therapeutic procedure, that is constantly effective in the disease. These physicians have found that the treatment of chronic infectious arthritis is best approached on a broad and comprehensive basis similar to that employed in tuberculosis. A therapeutic program directed towards improving the physical condition of the patient to the maximum degree is most apt to be successful in the majority of cases. It is with this approach to the disease that this article is concerned.

The number of remedies that have been recommended at one time or another as "sure cures" of arthritis would no doubt fill a single spaced typewritten sheet of paper as long as both outstretched arms. This fact in itself is testimony to the fact that there is no single remedial agent that is 100 per cent effective in combating this disease.

With this brief preamble it is well to define what is meant by the term infectious arthritis. The disease is known by a variety of synonyms, the more important of which are atrophic, rheumatoid and proliferative arthritis. No attempt will be made to outline the differential points between atrophic arthritis and the other forms of the disease. However, a discussion of the differential points between chronic infectious and hypertrophic (senescent, osteo-arthritis, degenerative, arthritis deformans) should prove of value, because it is with this joint disease that atrophic arthritis is most apt to be confused. Table I illustrates the differential points between the two conditions. A consideration of these points usually enables a differentiation between the two diseases to be made in most instances.

THE CLINICAL COURSE OF THE PATIENT WITH CHRONIC INFECTIOUS ARTHRITIS

If the clinical courses of one hundred patients with chronic infectious arthritis are followed until the termination of the disease, they may be divided into three distinct groups. Between 10 to 15 per cent of cases completely recover, apparently regardless of the therapeutic regimen employed. It is this group that is responsible for the wild speculations as to the value of different drugs and procedures in the treatment of the disease. These are the cases that are cured by orange juice diets, rheumatism bracelets, chiropractic adjustments, salicylate and iodide injections and similar procedures. A second group, fortunately comprising only about 10 per cent of cases, rapidly progresses to hopeless crippledom even though these patients receive the most excellent care. In these patients all therapeutic efforts fail to produce the desired results. Regardless of what is done, the progress of the disease remains unchecked and either causes early

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death or rapidly leaves them crippled for the remainder of life. The third group comprises the remaining 75 to 80 per cent of cases and includes the majority of persons with arthritis who come to the physician. Therapeutic efforts in this group are likely to be rewarded by a clinical improvement in a high percentage of cases. Chronic infectious arthritis in these patients may be said to be a disease that undergoes frequent spontaneous remissions and exacerbations. The physician should not be too quick to attribute an improvement in the arthritis to the particular drug or plan of therapy that was being used at the time of a remission. It is entirely possible that the disease may undergo a spontaneous remission at the particular time that a new remedy was begun. In the early stages of the disease these remissions occur frequently and tend to be more complete, that is, joint function tends more nearly to approach normal. As the disease progresses, remissions occur less frequently and are less complete. Each exacerbation in the severity of the disease leaves the joints more permanently disabled. Finally, after a variable period of time, probably averaging 15 years, the disease burns itself out and becomes inactive. The time required for the disease to run its natural course is exceedingly variable and ranges from a few months to as long as 25 years. In an average case it should be assumed that the disease will last about 15 years. After the disease runs its course the degree of function remaining in the affected joints is extremely variable and depends in great part on the amount of damage that occurred when the disease was active.

Joint symptoms in both treated and untreated arthritis are apt to become aggravated following menstruation, changes in the weather, on cold damp days, in the winter, following emotional disturbances, fatigue, and over-exercise of the affected joints. Too much attention should not be paid to the joint complaints from day to day.

WHAT CAN WE PROMISE THE PATIENT WITH CHRONIC INFECTIOUS ARTHRITIS?

The patient with chronic infectious arthritis should be told that in all probability the

TABLE I
DIFFERENTIAL POINTS BETWEEN ATROPHIC AND HYPERTROPHIC ARTHRITIS (HENCH)

Characteristics	Chronic Infectious Arthritis	Senescent Arthritis
Age at onset	Any age, usually below 40 yrs.	Usually 40-50 years
Body type	Any type, usually asthenic	Any type—usually obese
Prodromes (fatigue, exhaustion, anemia, weight loss, general malaise)	Usually marked	Not marked
Onset	Insidious but may be sudden	Insidious
Progression	Marked	Usually not marked
Joints affected	Many, peripheral in distribution	Few-weight bearing as a rule.
Joints spared	None may be	Elbows, wrists, knuckles, feet
Appearance	Spindle shaped due to swelling of joint and atrophy of adjacent muscles	Usually no findings except in terminal phalanges
Effusion	Common and great	Slight, if ever
Ankylosis	Common	Rare
Systemic manifestations (fever, tachycardia, low blood pressure, loss of weight, anorexia, anemia)	May be profound	Slight
Laboratory examinations		
Sedimentation rate	Increased	Normal
Filament-nonfilament count	Left shift	Normal

disease will last about 15 years and will eventually burn itself out and become inactive. Therapeutic efforts should be directed towards teaching patients how to force the arthritis to a lower level of activity so that when the disease does become inactive joint damage will be minimum and will leave the affected joints in a relatively good condition. The diseased joints will not be as good as normal joints but nevertheless will function for all practical purposes almost as well as normal joints. The word "cure" should never be used in discussing results in rheumatoid arthritis. It is much better to speak of an arrest of the process, or attempting to produce a remission, or forcing the disease to a lower level of activity. Very few of these patients experience a complete cure of the disease and it is best not to buoy up their hopes with unwarranted therapeutic claims.

In exceptional cases extraordinary results may occur in a few weeks or months; however, this is not the rule. The results of treatment in the disease should not be measured in weeks or in months. No great concern should be shown about how the patient feels today or this week but how he is improving from month to month. Improvement, if it is possible, is a slow and tedious process and is exhausting to both the patient and the physician. The patient should realize at the beginning of treatment that there is no one drug or therapeutic measure that gives constantly excellent results and the treatment to be outlined has withstood the test of time and has produced the best results in the long run. Such an explanation makes these patients more content with their slow progress and less likely to search for some other physician or cultist in the vain hope of securing a "sure cure" for their rheumatism. It is best to explain to these patients that if they do go from place to place seeking a complete cure they are losing their best chance of obtaining a remission in their disease. The longer the disease goes unchecked, the more joint damage results and the more severe the residual joint damage when the disease does burn itself out. The treatment of chronic infectious arthritis should be a long range program and is directed to extend over a number of years. Patients should be told that relatively simple measures such as diet, rest, removal of focal infection, transfusions, physical therapy, typhoid vaccine, arthrotropic vaccine, correction of postural defects, shoe corrections, joint exercises, and vitamin supplements should be tried first. After a thorough trial of these measures, additional therapeutic procedures are added if necessary. These include neoarsphenamine, gold therapy, sulphur, large doses of vitamin D, bee venom, iodides, iontophoresis, histamine, chaulmoogra oil and bilirubin. When patients realize that there is a host of "remedies" that may be used in the treatment of the disease and if one does not produce a remission another one may, confidence will be sustained. It must be impressed on them that any of these agents alone are ineffective and are likely to produce the best results in combination with the non-specific measures as outlined. The patient should be treated as a whole and not just the joints. Chronic infectious arthritis is a systemic disease and is no more a disease of the joints than typhoid fever is a disease of Peyer's patches. Efforts directed towards improving the patient's well being as a whole are most apt to be successful. The therapeutic program employed in arthritis is in this regard similar to that for tuberculosis and must of necessity be broad and comprehensive.

THERAPEUTIC MEASURES

An outline of these non-specific measures which are so valuable should be in order.

DIET

Regarding the question of what the patient with chronic arthritis should eat, Bauer has evaluated the following diets: (1) low carbohydrate; (2) reduced caloric intake; (3) altering the acid base balance of the diet; (4) omission of so-called acid fruits and vegetables; (5) allowing only one type of food substance at each meal; (6) omitting foods to which the patient is hypersensitive and (7) a low protein diet. He clearly demonstrated that there is no

good evidence to support the use of any of these diets in patients with rheumatoid arthritis. The concensus of most rheumatologists today is to allow the patient with chronic infectious arthritis the same diet that would be prescribed if the disease were not present.

About 75 to 80 per cent of persons with the disease are underweight, therefore the proper diet is one calculated to make them gain in weight, that is, a high caloric diet. The majority of arthritic patients suffer from constipation; the diet should therefore contain bulk producing substances calculated to relieve this condition. Because there is much evidence of a negative vitamin balance in many cases of rheumatoid arthritis, it is suggested that a high intake of these accessory food substances should be of value. The average person with chronic infectious arthritis therefore, will require a high caloric, high vitamin, anti-constipation type of diet. If the patient is overweight and is not too exhausted and anemic the diet should be one calculated to reduce the excess weight. This can be incorporated in a low caloric, high vitamin, anti-constipation diet. Reduction in weight should be carried out more slowly than in the average obese person, carefully noting any evidence of an aggravation of symptoms by the low dietary program.

REMOVAL OF FOCI OF INFECTION

It has been most interesting to note the changing views of persons interested in arthritis on the theory of focal infection. Twenty-five years ago, when the focal infection idea came into prominence it was hailed as the long sought cure of the disease. With the passage of time many of the former advocates of the theory have lost much of the faith that they had in the procedure. Cecil, at a recent meeting of the American College of Physicians in Cleveland, remarked that he was ashamed to state how long it had been since he had referred a patient with arthritis with apparently diseased tonsils to the ear, nose and throat department for tonsillectomy. In 1927 Cecil and Archer found that the majority of 200 patients with chronic infectious arthritis were improved by the removal of foci of infection. A similar survey in 1938 in the same number of cases led to the conclusion that only a few patients were benefited by the removal of infected foci. Cecil and Angevine conclude, "The time has arrived for a complete revaluation of the focal infection theory. Undoubtedly there are cases of infectious arthritis that result from focal infection. However, as far as typical rheumatoid arthritis is concerned, it would appear that chronic focal infection plays a comparatively unimportant role." Kinsella, Bauer, Dawson, McCollum and Shapiro concur in this opinion. Removal of so-called infected foci is frequently followed by a temporary improvement in the arthritis. This, in most cases, can be attributed to the non-specific effects of the anesthetic, rest in bed, restricted diet and the traumatism incident to the operation itself. In addition, removal of supposedly infected foci is in itself a major psychotherapeutic procedure that no doubt has a beneficial psychologic effect upon the patient with rheumatism.

Probably the attitude in these cases should be to remove obvious foci of infection with the idea that the absorption of theoretical toxins from such a focus may undermine the patient's resistance and render him less able to combat the disease. The patient should understand that mere removal of an infected focus will not cure the arthritis. If foci are to be removed at all this should be done early in the disease. Later removal of infected foci cannot be expected to have a permanent beneficial effect upon the arthritis. It is interesting to note that Kinsella believes that foci may be unrelated to the arthritis and are merely an accompanying disease, another manifestation of the lowered general resistance of the patient who allows infections to develop in joints, teeth or sinuses.

REST

Rest should be physical, mental and local. The majority of patients with the disease are weak, tired, run down and exhausted. In the acute stages of the disease, absolute bed rest is necessary for a variable period

of time, ranging from a few weeks to six or even eight months, depending on the severity of the case. A period of complete rest in bed early in the disease may prevent spending many months in bed later. As the disease lessens in severity, increasing periods of activity are allowed. Even when the patient is allowed a maximum amount of activity, a rest in the mid-morning and mid-afternoon and ten hours' rest at night should be insisted on. Fatigue is to be avoided at all times.

A recent study of the cause of acute exacerbations in arthritic symptoms by Cobb, Whiting and Bauer showed that emotional disturbances were apparently the exciting causes in 66 per cent of their 50 cases of chronic infectious arthritis. An effort should be made, therefore, to reduce emotional stress and strain to a minimum. Probably one of the most important factors concerned in the aggravation of symptoms is the belief of the patient that the disease carries with it a hopeless prognosis. Realization of the fact that between 75-80 per ment of patients can be definitely benefited by a proper therapeutic approach should lead to a decrease in this exciting factor. Every effort should be made to bolster morale and restore confidence without minimizing the seriousness of the disease.

Local rest of the joints is obtained by the use of light splints and plaster molded casts. The purpose of splints is primarily to prevent deformity. In the acute phases of the disease they are kept in place throughout the twenty-four hour period, except for a period of a few minutes during which the affected joints are carried through the full range of motion allowed before the appearance of pain. Splints are particularly useful at night because it is at this time that flexion deformities are most apt to begin. As the acute process subsides the splints may be removed for increasing longer periods of time.

PHYSICAL THERAPY

Physical therapy is merely an adjunct to other treatment in arthritis. Alone it does not cure arthritis and the use of this measure to the exclusion of other anti-arthritic treatment, does not produce the best results. However, it is probably the most important single procedure used in the treatment of arthritis. Its main value is to increase the blood flow to the affected area, thus aiding in the removal of waste products and hastening the absorption of inflammatory exudates. It also increases local nutrition, relaxes muscular spasm and often relieves pain. Types of physical therapy employed in arthritis are heat, massage and exercise. Heat may be applied in a number of ways as contrast baths, paraffin baths, heat lamps, infra-red lamps, electric bakers, diathermy, hot baths, cabinet baths, steam baths, mud baths and fever therapy. The valuable agent in all of these methods is heat and the form selected should be one that the patient is most likely to apply over a long period of time.

Many patients with arthritis have the delusion that joints must be exercised as much as possible in order to prevent stiffness. During the acute stages of the disease one or two gentle movements of the affected joints should be performed daily. In this manner dense adhesions and subsequent ankylosis are prevented. As the patient improves, the amount and the type of exercise is modified and increased. The golden rule governing the amount of exercise to be taken is that any motion, which is attended or followed within twenty-four hours by an increase in pain, swelling or stiffness in the exercised joint, is excessive. The proper time for both massage and exercise is after the application of one of the forms of heat previously mentioned.

FOREIGN PROTEIN THERAPY

This is one of the most valuable therapeutic agents that may be employed in the treatment of chronic infectious arthritis. The rationale of its use is that it may set into motion that vague mechanism known as the resistance of the host. Exactly how this is accomplished is unknown. Suffice to say, however, most patients with the disease will obtain symptomatic improvement following its use. In about 10 to 20 per cent of cases the improvement may be permanent; in the remaining cases the re-

mission will persist for several weeks or months. Typhoid vaccine is the agent most frequently used for this purpose. Intravenous vaccine should not be given to individuals above the age of 50 years because of the danger of vascular thrombosis. Foreign protein therapy is best given twice a week for a total of six to eight injections. The beneficial effect of intravenous typhoid vaccine may be prolonged if it is followed by the subcutaneous injection of streptococcus vaccine (preferably on arthrotropic strain) twice weekly over a period of three months. It should be noted at this point that several months may elapse before the full beneficial effect of foreign protein therapy is evidenced.

ACCESSORY THERAPY

Three or four transfusions of 300 c.c. each should be given if the red cell count falls below 3,500,000. Following these transfusions, some readily assimilable iron preparation, such as ferrous sulphate in doses of 15 to 20 grains daily, is useful. This drug is also indicated in milder degrees of anemia.

Cod liver oil, one ounce two to three times a day, two brewers' yeast tablets three times daily, cevitamic acid 100 mg. twice a day, are additional measures calculated to accomplish the vague purpose of increasing the resistance. Neoarsphenamine 0.3 gram once or twice weekly for ten doses may be used on purely empirical grounds to accomplish the same purpose. Insulin is frequently useful in patients who complain of anorexia.

In all cases attention must be paid to correct posture, flat or pronated feet. In flattening of the longitudinal arch of the feet the use of felt pads moulded to conform to the arch of the foot affords much comfort. In pronated feet the Thomas heel may be employed. Patients having painful metatarso-phalangeal joints are often benefited by having transverse metatarsal bars placed on the soles of the shoes. Proper fitting shoes with sensible heels should be insisted on. Ambulatory arthritics with painful knees frequently obtain much relief following the proper application of a three inch elastic bandage to the affected joints.

These more or less non-specific measures should be employed studiously over a period ranging one to six months, depending upon the response of the patient. At the end of this time both objective and subjective improvement should be evaluated and if a remission by suitable degree has not been obtained, one is justified in using one of the many less reliable procedures. These include the use of gold, bee venom, chaulmoogra oil, massive doses of vitamin D and fever therapy. When one of this last named group of therapeutic agents is used the former non-specific measures should not be abandoned but should be continued in addition to those more recently recommended. A combination of procedures is more likely to induce a remission in the activity of the disease and maintain it than any single measure that is now known.

SUMMARY

There is no single remedial agent that is constantly effective in the treatment of chronic infectious arthritis. Therapeutic measures, each of which alone has but little value, when combined frequently induce and maintain satisfactory remissions in the activity of the disease. The treatment of this disease should be a long range program, so arranged as to be conducted over a period of years. It should be on a broad and comprehensive basis similar to that employed in pulmonary tuberculosis. Therapeutic efforts directed towards improving the general physical condition of the patient are most likely to be successful in the largest number of cases.

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CLINICAL AND HEMATOLOGIC STUDIES IN SOME OF THE BLOOD DYSCRASIAS*

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One of the most interesting and certainly one of the most perplexing groups of diseases is the one usually referred to as the blood dyscrasias. Their increasing incidence can be explained in two ways. There is an apparent increase due to their more frequent recognition because of improved diagnostic facilities. There is a real increase, however, as the result of a more general use of chemical therapeutic agents in the management of the infectious diseases.

The importance of recognizing the blood dyscrasias in general practice is emphasized by the dramatic results obtained by specific therapy, particularly in the anemias. Yet few diseases present clinical pictures which are more bizarre, especially as regards the onset and clinical features of the early stages. Furthermore, many cases in which the history and physical findings are the same will prove to be entirely different hematologically, while identical hematologic pictures may be associated, at the outset, with clinical pictures varying from that of a mild infectious disease to that of a profound toxemia. Generally speaking, there are two important clinical features in the acute cases, necrotic ulceration, and persistent oozing or actual bleeding from the mucous membranes. Their presence in any given case simulating an acute infectious disease should at once arouse the suspicion that one is dealing with a primary disease of the blood or of the blood-forming organs.

The cases which are reported in this paper have been selected to illustrate certain clinical and hematologic observations which are important in various types of blood dyscrasia.

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ACUTE INFECTIOUS MONONUCLEOSIS

Case 1. L.L., a white male three years of age, was admitted to the contagious unit of Charity Hospital of Louisiana at New Orleans, September 25, 1938, with a diagnosis of gonorrheal ophthalmia, which was later confirmed bacteriologically. The patient was afebrile and looked healthy, and the physical findings, except for the eyes, were essentially negative. Urinalysis and the blood Wassermann reaction were both negative.

Treatment for the ocular condition was instituted and the course was without incident until October 20 (25 days after admission), when the temperature rose to 101° F. Examination showed a right cervical lymphadenitis, the nodes being firm and slightly tender, but not painful. The blood examination two days later (October 22) revealed 34,000 white cells with 71 per cent polymorphonuclear cells, 25 per cent lymphocytes, 1 per cent monocytes, and 3 per cent eosinophils. Roentgenologic examination of the chest was negative. The adenopathy was treated with warm moist compresses, but the low grade fever persisted.

November 4 a second blood study revealed 4,800,000 red cells, 85 per cent hemoglobin, 121,000 white cells, 79 per cent lymphocytes, and 16 per cent polymorphonuclear cells. Four days later (November 8) another blood study revealed 3,900,000 red cells, 82 per cent hemoglobin (12 gm.), hematocrit 34, and 128,000 white cells, practically all of which were mature small lymphocytes. The mean corpuscular volume was 87, the mean corpuscular hemoglobin 30, and the platelets 300,000. Repeated blood studies revealed little deviation from this hematologic picture. Urinalysis was consistently negative except for a trace of albumin.

November 16, 27 days after the initial rise, the temperature returned to normal and the lymphadenopathy subsided, though the blood picture remained practically unchanged. The spleen and liver were not palpable at any time during the illness. The patient was discharged with a diagnosis of gonorrheal ophthalmia, acute infectious mononucleosis, and possibly lymphatic leukemia.

December 7, 1938, the child was brought back to the hospital for a check-up. At this time the blood picture was within normal range, showing 7,900 white cells, 71 per cent polymorphonuclear leuko-

cytes, and 26 per cent lymphocytes. He was apparently perfectly well. He was also perfectly well when he was readmitted to the hospital December 19, for the treatment of a recurrence of the ophthalmia. On this occasion, as well as on March 22, 1939, when he entered the hospital with measles, hematologic studies revealed no abnormalities. On the last admission the heterophil antibody reaction was negative. The final diagnosis was probably acute infectious mononucleosis.

COMMENT

This case illustrates the difficulty in the differential diagnosis of lymphatic leukemia, acute mononucleosis, and pertussis. The latter disease was not seriously considered because of the absence of any respiratory symptoms of any kind. The diagnosis of acute lymphatic leukemia could not be substantiated because the child appeared quite well throughout his illness; there was no anemia, and ulceration, bleeding, splenomegaly and generalized lymphadenopathy were also absent.

In view of the findings, acute infectious mononucleosis seemed the most probable diagnosis. The heterophil antibody reaction[1], which is a most important diagnostic procedure in this disease, was not done at the time of the acute illness and the negative reaction three months later is not considered of great significance because of the time which had elapsed.

ALEUKEMIC MYELOID LEUKEMIA

Case 2. C.D., a white female 15 years of age, was admitted to Hotel Dieu service of Dr. J. E. Landry, November 4, 1937, complaining of pallor, weakness, and bleeding gums. She had been treated for the latter condition by a dentist for several weeks before admission. She had become progressively weaker and paler until a week before admission, when the gums became very sore and persistent bleeding occurred.

The temperature was 100.6° F., the pulse rate 120, and the respiratory rate 28 per minute. The blood pressure was 110/50. The patient weighed 102 pounds and was fairly well developed and nourished, but was pale, restless, and apparently acutely ill. Physical examination was essentially negative except for continuous oozing from the gingival membranes and the vagina. There was no lymphadenopathy, and the liver and spleen were not palpable.

Urinalysis was negative except for a faint trace of albumin and many red blood cells. The blood chemistry was within normal limits. Gastric analysis showed hydrochloric acid 45° and total acidity 65°. Blood study revealed 1,400,000 red blood cells, 30-35 per cent hemoglobin, 2,000 white blood cells, 82 per cent lymphocytes, 17 per cent neutrophils, and 1 per cent myelocytes. Anisocytosis, poikilocytosis, polychromatophilia and basophilic stippling were present. Following a transfusion of 300 c. c. of blood the day after admission (November 5) the white blood cell count was 9,000. Examinations for malaria revealed no plasmodia. The fragility test was normal. Roentgenologic examination of the chest, November 7, was negative except for the presence of bilateral cervical ribs.

Five days after admission (November 9) clinical anemia was more marked and the white blood cell count was 8,000. For the first time 13 per cent of the white cells were myeloblasts. Twenty-one days after admission (November 25) the white blood cell count was 7,750, with 20 per cent myeloblasts, 44 per cent myelocytes, 28 per cent lymphocytes, and 8 per cent mature neutrophils.

A diagnosis was made of aleukemic leukemia of the myeloid type. The patient continued to run a septic temperature varying from 101° to 103° F., with elevations to 104.5° F. following the five blood transfusions which were given. Other therapy included intramuscular injections of liver extract, pentnucleotide, and vitamin C, in addition to routine treatment. Death occurred November 29, 25 days after admission. Bone marrow aspiration was done immediately after death. The reddish-gray marrow proved on microscopic examination to be acute myeloid leukemia.

COMMENT

This case is an excellent illustration of the difficulty in differential diagnosis between aleukemic leukemia, which is merely an early acute leukemia before manifestations are present in the peripheral blood stream, and agranulocytosis. The clinical picture and relative neutropenia in the peripheral blood would certainly suggest agranulocytosis, but the diagnosis of the aleukemic phase of an acute myeloid leukemia would seem to be substantiated by the rapidly developing thrombocytopenia and anemia in the presence of increasing numbers of embryonic white blood cells of the granular series in the peripheral circulation. A specimen of bone marrow obtained by sternal puncture would have furnished the necessary confirmatory evidence in this case, but permission for the procedure could not be obtained during life.

ACUTE MYELOID LEUKEMIA

Case 3. Mrs. O. R., a white female 38 years of age, was admitted to Hotel Dieu, service of Dr. Val Fuchs, October 10, 1938, complaining of sore

throat and pain on swallowing. The illness had begun a week before admission as a mild sore throat and fever, associated with dysphagia, which had become progressively worse. The onset of illness had coincided with the onset of menstruation, and the flow had become excessive. The history was otherwise irrelevant.

The temperature on admission was 102°F., the pulse rate 120 and the respiratory rate 25 per minute. The blood pressure was 100/50. Physical examination revealed a well developed and well nourished white female who was very toxic and apparently acutely ill. The breath was foul. The gingival and oral mucous membranes were pale, and a fragile, spongy, bleeding mass, about 2 cm. in diameter, was seen on the left side of the roof of the mouth. The heart and lungs revealed no abnormalities, and the spleen was not palpable. The menstrual flow was excessive.

Urinalysis (catheterized specimen) revealed 2 plus albumin and much blood. The blood chemistry was within normal range. Blood study revealed 2,000,000 red cells, 29,000 white cells, 68 per cent myeloblasts and myelocytes, 16 per cent juvenile cells and 1 per cent stab cells. Direct smear and culture of the throat were positive for *C. diphtheriae*.

Sulfanilamide in adequate doses was begun, and 20,000 units of antidiphtheritic serum was administered. The patient also received five transfusions, and was given neosalvarsan and deep x-ray therapy over the spleen and the long bones.

Blood study November 3 (24 days after admission) revealed 1,790,000 red cells, 162,250 white cells, and 90 per cent myeloblasts. Repeated blood cultures were negative.

All therapeutic measures were without benefit and the patient died November 4. Autopsy examination, which was limited to aspiration of the bone marrow, confirmed the diagnosis of acute myeloid leukemia. The final diagnosis was acute myeloid leukemia and probable diphtheritic carrier.

COMMENT

The point of chief interest in this case is perhaps the similarity of the clinical picture to that of any other sore throat which might be seen in general practice. It is particularly significant that diphtheria organisms were present in large numbers in the lesion. The acute infection undoubtedly could account for the severity of the symptoms, but the profound toxemia and spreading necrotic ulceration strongly suggested the lesion to be one of leukemic origin. The suspicion was promptly confirmed by the hematologic studies made at this time.

The question is frequently asked whether x-ray therapy could possibly change an acute leukemia into one of chronic character, and thus prolong life. This measure was employed in this case, in addition to transfusions, but was entirely without effect.

MACROCYTIC HYPERCHROMIC ANEMIA

Case 4. A. R., a white female 52 years of age, was admitted to Charity Hospital of Louisiana January 2, 1939, complaining of weakness, diarrhea, and shortness of breath. For the past six years she had had recurrent attacks of diarrhea. The stools had been formed and grayish in color until quite recently, when they had become offensive in odor and were described by the patient as "foamy like beer." Her skin had become very pale and she said that her tongue was sore and "red as a beet." For the past year she had had cramping pains in her legs, dizzy spells, and dyspnea on exertion. She had lost 40 pounds during the past few years. The remainder of the history was irrelevant, except that she had become completely gray at the age of 40 years and had reached the menopause at the age of 45 years.

The temperature on admission was 98.6°F., the pulse rate 86, and the respiratory rate 18 per minute. The blood pressure was 110/70. Physical examination revealed an emaciated, ambulatory individual who looked at least 80 years of age. Although she was chronically ill, she was alert and cooperative. She weighed 82 pounds. The skin was dry, thin, wrinkled and lemon-colored. The pupils reacted to light and accommodation. The tongue was red, smooth and atrophic. Examination of the heart and lungs revealed nothing abnormal. The abdomen was distended and of the "pot-belly" type. The reflexes were generally diminished but symmetrical. The tentative diagnosis was sprue, pituitary cachexia, and premature senility.

TABLE I

Day	5th	10th	27th	43rd	59th
Hgb. gms.	3.8	5.5	10	11	
WBC	6,200	4,400	7,100	4,500	
RBC	1.1	1.3	2.87	2.8	3.1
Hmtcr.	12	15	30	27	
M.C.V.	109	115	105	98	
M.C.H.	34	42	35	40	
Retic.%	2.4	12*			

*After administration of 5 c.c. liver extract daily. Note reticulocyte response.

The blood Wassermann reaction was negative. Urinalysis revealed urobilinogen 4 plus, urobilin, and traces of sugar and albumin. Three consecutive stools were gray, foamy and greasy, and contained many fatty acid crystals and some mucous and pus, but no blood.

The icterus index was 10. Blood chemistry studies revealed 7.7 mg. of urea nitrogen, 88 mg. of glucose, 6 mg. of calcium, and 2.37 mg. of phosphorus per 100 c. c. Gastric analysis revealed free hydrochloric acid 15° and total acidity 25°. After the administration of histamine the values were re-

spectively 52° and 79°. Neurologic consultation one week after admission resulted in a diagnosis of posterolateral sclerosis secondary to anemia.

Agglutinations for bacillary dysentery were negative. Castellani's rhamnose test (4 gm. orally) showed no sugar in the urine during a six hour period.

Insulin hypersensitivity test January 12 (10 days after admission) was markedly positive following injection of 10 units of insulin. The fasting blood sugar was 88 mg. per 100 c. c. At 30, 60 and 90 minutes after the injection the blood sugar level was too low to read. At the end of two hours the blood sugar was 69 mg. per 100 c. c. The test was repeated January 28 with approximately the same results. February 2 the fasting blood sugar was 90 mg. per 100 c. c. of blood. Thirty minutes after the ingestion of 100 gms. of glucose it was 111, and at 60 minutes and 120 minutes it was respectively 95 and 90 mg. per 100 c. c. The glucose tolerance test was repeated March 6, with similar results.

Roentgenologic examination of the long bones showed no abnormalities. A basal metabolic rate determination one week after admission was plus 22, and 18 days later was plus 31.

January 22 (20 days after admission) sternal puncture revealed active marrow with definite erythroid cell stimulation. The normoblasts were seen in different stages of development, although no megaloblasts were identified. There were many myelocytes and premyelocytes.

Two months after admission and after parenteral liver extract therapy the patient weighed 115 pounds, a gain of 33 pounds. She felt much stronger, the diarrhea had subsided, the red blood cell count had risen from 1,100,000 to 3,100,100, and she seemed entirely recovered.

The final diagnosis was macrocytic hyperchromic anemia (sprue) probably due to lack of absorption of the intrinsic factor of the stomach.

COMMENT

The diagnosis seemed to be confirmed in this case not only by the presence of anemia and its response to parenteral liver extract, but also by the presence of fatty, foamy diarrheal stools and of central nervous system lesions. The lack of absorptive powers on the part of the duodenum was demonstrated by Castellani's rhamnose test.

Just what mechanism, other than sprue, produced the syndrome present in this patient is an interesting question. Atrophic cirrhosis of the liver, as in Simmonds' disease, might perhaps explain it, but no demonstrative evidence of this state could be elicited, and the result of the glucose tolerance tests and the absence of clinical jaundice and of ascites tended to refute its possible existence.

An interesting comment regarding the apparent anterior pituitary deficiency in this case has been made by Bauer[2]. He presented evidence to show that the deficiency syndrome resulted from a lack of absorptive powers on the part of the duodenum which resulted in a starvation process despite the oral administration of food.

APLASTIC ANEMIA

Case 5. Mrs. C. A., a white female, 28 years of age, was admitted to Touro Infirmary, service of Dr. J. D. Rives, November 24, 1938, complaining of profuse nose bleed, excessive menstruation, and the appearance of "blood spots" all over her body. Six months before admission she began to grow progressively weaker and to suffer from frequent fainting spells. At the same time the mild menorrhagia and anemia from which she had suffered for four or five years became considerably worse. Menstruation occurred every 21 days and an excessive flow lasted from seven to nine days. All treatment of the anemia, including the use of liver extract, was without avail, though slight temporary improvement followed several blood transfusions two months before admission. Two days before she entered the hospital bleeding from the mouth began to occur and the "blood spots" mentioned developed beneath the skin. The previous history revealed no exposure to drugs or x-ray therapy, or any other possible cause of the illness.

The temperature on admission was 101°F., the pulse rate 110 and the respiratory rate 24 per minute. The blood pressure was 110/60. Physical examination revealed a white female who was very ill and apprehensive and whose skin had an ashen pallor. There was a constant slow oozing of blood from the nose, gums, and oral mucous membranes. The chest findings were negative except for the presence of a tachycardia. The liver and spleen were not palpable. There was a profuse oozing of blood from the vagina. There were numerous purpuric spots over the extremities. The reflexes were normal and no lymphadenopathy was present.

The tentative diagnosis was purpura hemorrhagica. The patient was given a blood transfusion and 2000 units of theelin intramuscularly. Morphine was also administered.

Urinalysis (catheterized specimen) revealed 1 plus albumin and many red blood cells. Examination of the stools was negative except for 4 plus occult blood. The gastric analysis revealed no free hydrochloric acid and total acidity of 15°; gross and occult blood was present. Blood study showed 2,620,000 red cells, 50 per cent hemoglobin, 4,200 white cells, 48 per cent neutrophils, and 52 per cent lymphocytes. The platelet count was 10,000

per cu. mm. The bleeding time was over two hours. Clot reaction did not occur. The tourniquet test was positive.

Sternal puncture November 29 (five days after admission) revealed 8,000-10,000 nucleated cells, 6 per cent granulocytes, 29 per cent lymphocytes, 2-4 per cent reticulocytes, 42 per cent nucleated red blood cells, and markedly decreased platelets.

A diagnosis of thrombocytopenic purpura, due to aplastic anemia, was made. The patient was treated with 16 transfusions of whole blood, vitamins D and C, koagmin, coagulin, calcium gluconate, thromboplastin, liver extract, pentnucleotide, snake venom, gynergen, and deep x-ray over the pelvis.

Although no beneficial effect was expected from it, splenectomy was performed December 11, 18 days after admission. The patient continued to bleed after operation and died December 22, 1938. Postmortem confirmed the diagnosis of aplastic anemia and thrombocytopenic purpura.

COMMENT

This case is of unusual interest because of the lack of any factor to which the fatty degeneration of the bone marrow could be attributed. That the bone marrow changes represent a primary pathologic phenomenon must be granted. Such a phenomenon, however, is most unusual. Although all therapeutic measures were carried out to an adequate degree over a sufficiently long period of time, all were without benefit, with the possible exception of the transfusions.

A recent report by Osgood and his associates[3] concerns an attempt at transfusion with the addition of bone marrow in a case of aplastic anemia. Although the results in their particular case were not good, the method suggests possibilities for the future. Since no known method of treatment is of any permanent benefit in the so-called primary aplastic anemias, it may be that bone marrow transplantation from a healthy, normal individual, of identical type, would be worthy of future trial.

SUMMARY AND CONCLUSIONS

1. The apparently increasing incidence of diseases of the blood and of the blood-forming organs seems particularly important in relation to the advent and increasing use of specific chemotherapy in the acute infectious diseases.

2. It is important that routine hematologic examinations be undertaken in all cases of necrotic ulceration or persistent oozing of blood from the mucous membranes.

3. Five cases of blood dyscrasia are reported and commented upon in this communication: (1) Acute infectious mononucleosis simulating chronic lymphatic leukemia; (2) aleukemic leukemia simulating agranulocytosis (agranulocytic angina); (3) acute myeloid leukemia simulating necrotic ulceration of the palate caused by diphtheria and possibly Vincent's organisms; (4) sprue with anterior pituitary deficiency simulating pernicious anemia and adrenal insufficiency or Simmonds' disease; (5) idiopathic aplastic anemia simulating acute thrombocytopenic purpura.

4. Important diagnostic information can be secured in cases of suspected blood dyscrasia by biopsy studies of sternal marrow, in addition to routine hematologic examinations.

Note: Our thanks are due to Drs. Jerome E. Landry, Val Fuchs, and J. D. Rives for permission to report three of the cases in this group.

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DISCUSSION

Dr. John H. Musser (New Orleans): I want to stress the importance of the examination of the throat, and more particularly, the importance of making blood counts in people who show abnormal conditions of the throat. Dr. Tripoli has pointed out that mucous membrane lesions may occur anywhere with peculiar blood pictures and blood dyscrasias. It is perfectly obvious that the easiest membrane to observe is the mucous membrane of the mouth and throat. Illustrative of the fact that it is of a certain amount of importance is an incident which occurred at Charity Hospital some few years ago. I went on my vacation, and just prior to going I talked about this matter with Dr. Weilbaecher, who was taking over the care of the contagious ward as chief house officer, and he said that he would insist that a leukocyte count be made on every child coming in who had Vincent's angina, or ulceronecrotic lesions of the mouth, or had an acute inflammatory condition of the mouth. And in six weeks he had collected seven cases of children who had lesions of one type or another, and whose fundamental condition was due to their abnormal blood, or blood elements. A few years before that, I had written a paper and summarized

conditions which are associated with alterations in the leukocytic picture and associated with mouth conditions. If you do not mind, I would like to review that briefly.

First, there are mouth conditions which are associated with polymorphonuclear increase. These conditions are quite common. Those showing a blood reaction include such conditions as streptococcic sore throat, acute tonsillitis, or quinsy. I want to point out as of diagnostic importance that in diphtheria the large mononuclears are increased proportionately, much more so than you would expect with hyperleukocytosis.

The second is mononuclear increase. Here, there is infectious mononucleosis, which Dr. Tripoli illustrated, and a condition which is almost invariably associated with sore throat. As a matter of fact, sore throat is an ever present complaint in most of these younger people who have infectious mononucleosis.

Third, there is leukopenia with hypogranulocytosis. Here there is agranulocytic angina, which is, of course, associated with a very definite throat picture, and then occasional cases of Vincent's angina—Vincent's angina which I would like to speak of as systemic, in contradistinction to local Vincent's angina. At times, there is local throat involvement when there is aplastic anemia, and then occasionally, with severe sepsis it is possible to have lesions of the throat and to have leukopenia and hypogranulocytosis.

Fourth, is leukocytosis and relative hypogranulocytosis. This is the picture seen at times in acute leukemia, for example, and here again there is this particular picture sometimes produced in severe oral sepsis and whooping cough. The late Dr. Quinn of Shreveport reported a patient who had a horrible mouth, yet when the case came to autopsy they found nothing to explain the leukocytosis of over 40,000 cells. I want to point out that there is an abnormal blood picture in whooping cough, and sometimes very pronounced alteration takes place. Some years ago Dr. Krumbhaar wrote a paper on leukemoid reactions in various types of disease, and whooping cough was a splendid example. It is not necessary to point out to you that throat involvement in whooping cough is quite uncommon, but on the other hand, the child does at times have a sore throat from coughing. The particular case most vivid in my mind was one in Charity Hospital. This patient had a leukocyte count of over 120,000, and the child was kept on the ward for many weeks, and gradually after the subsidence of the whooping cough, the blood count came down to normal.

I would like to stress again that given a patient who has a sore mouth, a sore throat, do not dismiss the diagnosis perfunctorily as some local condition such as Vincent's angina. It happens so frequently in acute leukemia, that a leukocyte count, a total and differential, is made and then sometimes you will be surprised at the result of the hematologic study.

Dr. Joseph Stasney (New Orleans): I wish to confirm Dr. Musser's remarks as to the importance of the leukocyte count in blood dyscrasias and to add certain points as to the importance of the morphologic study of the individual white cell. Diagnosis is likely to be very difficult if only the number of white cells be considered. It is known that there is a normal fluctuation in the number of the leukocytes, and Doan and others have demonstrated that there is also a normal variation in the various types of white blood cells. These normal variations will naturally be exaggerated in pathologic conditions.

A blood dyscrasia is not primarily a disease of the blood itself but of the blood-forming organs. The blood merely mirrors the changes in them. In this connection Gullen said that in the future the study of the morphology of the individual blood cells will probably be as important as auscultation of the heart is in other diseases. Leukemia can easily be recognized by a study of the morphology of individual white blood cells; the number of the cells is unimportant, but their quality is very important.

I should also like to emphasize the importance of bone marrow puncture in the diagnosis of blood dyscrasias. For diagnostic purposes the sternal bone marrow is most readily available, and sternal puncture is not a difficult procedure.

The question arises, however, as to whether marrow found in the sternum is representative of the entire marrow, especially in view of the fact, which many authors have pointed out, that the cellularity of the marrow differs enormously. It is known that there are two kinds of bone marrow, red or cellular and yellow or fatty. Red marrow is found in the flat bones and fatty marrow in the lower two-thirds of the long bones. In the fatty marrow, however, are scattered foci composed of hematopoietic cells, which are seemingly active and which are surrounded by fatty tissue. Even though it be granted that the cellularity varies greatly according to the site from which the marrow is secured, the trend of the differentiation is the same in any given marrow specimen. In studies made at the Mayo Clinic, Dr. Higgins and I found that if the sternum showed erythrocytic stimulation, the same process could be demonstrated in marrow samples obtained from the femur, the rib, or any other bony structure.

Although sternal puncture is the easiest procedure for examination of the bone marrow, the admixture of peripheral blood, unfortunately, cannot be avoided. Surgical exposure of the marrow is another possible method, and undoubtedly excising a specimen, making a tissue preparation and studying the cells furnish more accurate results. On the other hand, simple sternal puncture can be repeated many times while surgical procedures cannot be repeated more than once or twice.

In conclusion, I should like to emphasize again the importance of careful morphologic studies which will help us to understand the correct nature of the various blood dyscrasias.

Dr. Allan Eustis (New Orleans): This paper has been most interesting to me. I recall a case I saw with Dr. Trepagnier, with typical agranulocytosis. The reason that I question that diagnosis now, is it was before the time of pentnucleotide.

She recovered with salvarsan and numerous transfusions. She was a friend of Dr. Elizabeth Bass, and six months later, Dr. Bass telephoned me the patient had a leukemia, white cells 150,000. I do not remember the differential count. Dr. Bass watched her for three months when she went to Boston and died there of typical leukemia. Was it not possible that she had acute aleukemic leukemia and not agranulocytosis?

Dr. Carlo J. Tripoli (In closing): The remarks made by Dr. Musser regarding the clinical features in these diseases and the importance of routine hematologic examination are both valuable and timely.

Further, the value of diagnostic sternal puncture cannot be overemphasized. The importance of sternal puncture is obvious. In a case of suspected blood dyscrasia where the blood picture results in no conclusive evidence, bone marrow studies will often reveal the correct diagnosis. The diagnostic information obtained by sternal puncture, the simplicity of the procedure, the lack of danger, all recommend it.

In regard to Dr. Eustis' case, sternal marrow studies at the time when the blood studies were inconclusive, would have proved the case to be one of leukemia without peripheral blood findings as is frequently seen in aleukemic leukemia during the early stages of the disease.

The use of x-ray therapy in two patients with acute leukemia proved ineffective.

Bone marrow transplantations in the treatment of primary aplastic anemia have been unsuccessful so far.

THE APPLICATION AND INTERPRETATION OF THE FRIEDMAN MODIFICATION OF THE ASCHHEIM-ZONDEK TEST*

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While the observations herein presented deal with the application and interpretation of results, obtained by employing the Friedman modification, it is felt that the discovery of Aschheim and Zondek[1] must be duly emphasized. Too often, unfortunately, originators or discoverers fall into oblivion because of some simpler or more popular changes in the original discovery made by follow-up workers. This assertion is not meant to deprecate the value of simplification through which such tests can be much more readily applied. On the contrary, such augmentations serve to place the test upon a more valuable basis. Friedman[2, 3] primarily noted the effects of urine of pregnant women upon the ovary of rabbits. This observation was later applied, from the practical standpoint by Friedman and Lapham,[4] in 125 instances. It is to be recalled that prior to the thorough and accurate observation, discovered by Aschheim and Zondek in 1928, numerous other procedures, including those of Abderhalden, Allen and Doisy,[5] Siddall,[6] Crew,[7] and Kanter, Bauer and Klawans,[8] had been found either too technical or too inaccurate to be of practical use. It is especially because of this latter factor, that is practicability, that the test as applied by Friedman and Lapham has become so generally employed.

Since the Aschheim-Zondek test for pregnancy has proved conclusively, over these many years, to be an accurate and valuable procedure, it is but just that their names be emphasized, independent of the various modifications that have subsequently arisen. For an excellent resumé of the literature, in addition to other important factors concerned herein, the publication of Stadiem[9] is very worthy of reference.

In connection with the application of this very valuable test, we are confronted with the factors which bring about its production. It is not intended herein to delve into extensive detail of the various hormonal substances concerned, but it does seem pertinent to refer briefly to the varieties that occur in regard to both the ovary and the anterior lobe of the pituitary body. These may be primarily divided into the estrogenic and gonadotropic substances.

*Read before the sixty-first annual meeting of the Louisiana State Medical Society, April 24, 1940, ta New Orleans.

In regard to the influence of the pituitary gland upon ovulation, the report of Pencharz, Cole and Goss, is of much interest. In their observations upon hypophysectomized rats, they noted that the injection of highly purified extracts of pregnant mare serum produced, grossly, many ripe follicles with some corpora lutea. Microscopic study confirmed these findings. At the same time, they noted that injection into male rats showed strong interstitial cell response as indicated by the response of the accessory organs. Whether or not these experiments have any bearing on the human species is not discussed.

It is to be emphasized that those substances recognized as definite factors in the production of estrus or menstruation, while constantly increasing with development of pregnancy, reaching as many as 20,000 mouse units at the time of delivery, are, however, not responsible for the test reactions produced in animal ovaries. On the other hand, the gonadotropic substances, that appear within a few days after the missed menstruation due to pregnancy, are present in the blood and urine in large amounts. It was upon this observation that Aschheim and Zondek formulated their very valuable test for pregnancy.

The principle of the test is the demonstration of the unusual increase of the gonadotropic substance. Using the infantile mouse, Aschheim and Zondek[10] found three definite changes in the ovaries of these animals: (1) Large mature follicles, which are capable of producing an estrogenic hormone: (2) numerous corpora lutea which either enclose the ovum or result from ruptured follicles; and (3) large blood-containing follicles. Microscopically, they differentiated three definite reactions: (1) Follicular maturation, that is formation of large follicles with secondary estrus; (2) hemorrhage in the follicles; (3) formation of corpora lutea with imprisonment of the ovum. The first reaction is considered physiologic, while the second and third are pathologic.

In connection with the various hormones that have been recounted, it is of interest that among these there is no one specific substance for pregnancy. It becomes a fortunate fact, however, that because of the marked increment of certain of the hormones excreted in the urine in pregnancy, such quantities are capable of registering very definite and specific results upon animals. To be more explicit then, the small amounts of such substances that may occur normally in both male and female urines are insufficient to bring about reactionary changes in the ovaries of the animals. The test, therefore, is definitely based upon a quantitative rather than a specific qualitative factor. For example, in the non-pregnant female, the urine will show 16 rat units per liter of the gonad stimulating substance while in pregnancy from 5,000 to 20,000 or more units per liter may be found throughout the entire term. It is of further interest that these substances disappear in from 48 to 96 hours after birth, except wherein chorionic tissue has remained connected with the uterine wall.

It is to be remembered that it is the exchange of material between the uterine circulation and the chorionic epithelial tissue that makes possible the urinary excretion of a sufficient volumetric amount to produce the test.

APPLICATION AND INTERPRETATION

The application of the test as herein reported does not represent the scientific observations upon positive results obtained in definite pregnant women as contrasted to those known to be negative. It deals rather with the following topics:

1. *"Problem Cases."* By such is meant the very early instances in which a missed menstruation has confronted the physician for interpretation as to whether or not pregnancy exists. It is quite surprising in private practice how many such instances of legitimate anxiety aside from those necessarily alarmed illegitimately in reality, present themselves. From the legitimate aspect, numerous married women demand definite information as to possible pregnancy even after the first missed menses. This they do for various reasons. Either they are hopeful they are not pregnant, either for no good, or good reason, such as ill health or

many children, or, occasionally, they are anxious to have a child. From the illegitimate standpoint, it can naturally be appreciated that it is most important to the woman or both the man and the woman to ascertain with all possible degree of certainty as to whether or not pregnancy exists. Sometimes a hasty marriage, from an overzealous courtship, ensues and at other times the prospective mother disappears, after the reassurance of definite pregnancy, not to be seen further by the physician unless subsequent complications arise; in other words, an abortion has been performed. Confronted with all of these very serious problems, even the most skilled obstetrician is quite inclined to be noncommittal at such an early period and naturally the employment of an accurate test serves a most useful and highly satisfactory purpose. The vast majority of tests have been derived from this category of problem cases in contrast to that type of case presented in hospital observation.

2. *Extra-uterine pregnancy.* Needless to say, wherein an extra-uterine pregnancy has brought about an abdominal crisis with an associated hemorrhage and some shock, no such test is indicated; in fact, delay by such a test is to be condemned. If, however, the clinical aspect suggests such a possibility, this test at once offers a valuable aid. It is to be noted that only wherein the living chorionic epithelium still exists, will a positive result be produced. It is really such a type of case wherein such information is more important inasmuch as rupture and hemorrhage from continual growth will eventuate. On the other hand, when intratubal hemorrhage and pressure have brought about the destruction of the abnormal pregnancy factors, comparatively little danger threatens the patient. Such occurrences, of course, will yield a negative result. With these facts in mind, therefore, if there has been primarily registered a positive finding with no intervention and subsequently a negative result has been obtained, it indicates the tubal pregnancy has discontinued growth. Of course, it is only a subsequent operative procedure that determines the presence of an extinct tubal pregnancy.

3. *Miscarriage.* In the instances where hemorrhage has occurred during an early pregnancy the question of whether an actual miscarriage or termination of pregnancy has eventuated occasionally presents itself. This is particularly applicable when the expelled specimen is not available for a proper microscopic examination. I have had the occasion to obtain positives before such bleeding and subsequently to obtain in some instances negative results and in still others positive results. The deductions drawn were, in the instances of the negative results, that miscarriage had occurred; in others that pregnancy had continued. These findings were confirmed by the eventualities of the cases.

4. *Fetal viability.* Among the tested cases of our series, there has been a small group wherein the question of fetal death has arisen. In one of these instances, the obstetrician considered that the fetus had died, and it was interesting to note upon the three successive tests that the reaction was primarily of a two-plus character, then of a one-plus character and finally yielded a negative result. This defervescence of reaction was attributed to the gradual death of the chorionic structure. The patient eventually aborted a dead fetus.

5. *Intra-uterine tumors.* As is well known, this test is applicable particularly to the diagnosis of the hydatid mole and the chorionepithelioma. Because of the fact that such types of growth permit of the output of the gonadotropic hormone in very considerable amounts, the urine of such subjects yields a very distinctly positive reaction. The failure to obtain a positive reaction in connection with a suspected pathologic pregnancy of these types, is more reassuring in excluding such possibilities.

6. *Chorionepithelioma of the male and teratomatous tumors of both sexes.* There has accumulated a considerable number of reports of definite positive reactions in such occurrences. In my experience, I have had but very few suspected instances which

proved both negative from the test and operative standpoint.

7. *False positives.* Stadiem,[9] in his publication, reports nine false positives consisting of three ovarian cysts (retention), one each of pituitary tumor, hypernephroma, ovary granulosal cell tumor and carcinoma of the uterus, and two of menopause. He also cites certain other similar factors such as hyperthyroidism, reported by other observers. Most of these observers have handled institutional cases and through this means, their reports are of great value. I have not encountered any false positives in particular types of cases. In this connection, it can naturally be understood that patients receiving certain endocrine treatment or extracts thereof are liable to yield a false positive result.

8. *False negatives.* From the false negative standpoint, it is to be appreciated that two factors are concerned: (1) The failure of sufficient titer of hormonal output in the urine, and (2) a refractory or immature rabbit. Of a group of ten false negative reactions, five yielding negative reactions ten days after the first missed menstruation, yielded definite positives within two weeks thereafter. Of the remaining five, most of which were repeated and persisted in negative results, three of the mothers later proved to be pregnant were between 40 and 45 years of age. The other two are inexplicable. In these instances, no chemical assays of the urine were made.

SUMMARY

While it is appreciated that there is nothing new that has been added in the present paper, on the other hand, because of the large number of tests that have been carried out (approximately 2500) particularly of the "problem variety," it is felt that its presentation is justified. The percentage of errors obtained has been approximately 0.5 per cent. This has been performed at the very early stage of questionable pregnancy, that is, shortly after the first missed menstruation. Beyond this, its application in potential extra-uterine pregnancy, possible fetal death or miscarriage has yielded valuable information.

In conclusion, this series of observations indicates that the Aschheim-Zondek test as modified by Friedman and first applied by Friedman and Lapham constitutes a most reliable and useful factor in the armamentarium of obstetric practice.

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DISCUSSION

Dr. E. L. King (New Orleans): The first point is the question of the negative reaction early in a suspected pregnancy. The reaction does not always become positive within a few days after the missed menstrual period but may be negative at this time and become positive later on. Positive reports have been made on patients who have not missed a menstrual period, that is, who are only two or three weeks pregnant, but that is exceedingly rare. In cases only a week or ten days past the menstrual period, do not make the mistake of running the test unless the patient is very insistent; if it comes back positive then you do know the patient is pregnant, but if it comes back negative, you still do not know.

Dr. Friedrichs brought out the value of the test in ectopic pregnancy. That is particularly true when the pregnancy is still alive in the tube. If

the fetus has died and the chorionic villi are no longer active there may be a negative test and still diagnosis of ectopic pregnancy will be correct. In a positive test you can suspect ectopic pregnancy.

In miscarriage again it is of value, and also in cases where there has been some bleeding and there is the question as to whether the fetus is still alive. Some of these women may bleed only slightly and then stop bleeding. In such cases the fetus may die and still be retained, thus a negative test may be obtained. In the matter of the life or death of the fetus, which is a subject of considerable concern, one thing brought out by Dr. Friedrichs is the duration of the test period on the rabbit. In one particular case the rabbit at the end of 48 hours was negative. We were very anxious to make sure before emptying the uterus, and at the end of 72 hours the test was positive. If we had acted upon the first report, we would have emptied the uterus of a live pregnancy. Therefore, in case of doubt, sew the rabbit up and wait. If the test becomes negative later it will carry the implication that the fetus has died. I have had some cases where there was definite death of the fetus with persistent positive reactions, which was explained by the fact that there were still live chorionic villi.

A good deal of work has been done on hydatid mole and chorionepithelioma from the quantitative standpoint, using ½ c. c. or less of urine for the test, but that has been inconclusive. While it is of some value, it has not been found to be accurate.

Regarding false positives, I may say I have known only two false positives and in each instance there was question as to whether the rabbit had been properly isolated. It is very important that these rabbits should be isolated before the test is run. At Tulane, the rabbits are put away for six weeks and they are isolated for four or five weeks after using before being used again. It is very important that this be done, otherwise you will get false positives. False negatives, as Dr. Friedrichs brought out, may be due to the fact that the rabbit does not react. In that case you have to use another rabbit.

Dr. M. L. Stadiem (New Orleans): I would like to agree with everything that has been said and would like to congratulate Dr. Friedrichs on his 0.5 per cent false negatives, which will correspond with that of the best clinics in the world—that is exactly what their percentage of false negatives is.

I would like to bring a few practical points to your attention, especially about the quantity of urine. One thing we have been overlooking is the type of urine. If the patient has a low specific gravity and puts out 4000 or 5000 c. c. a day it is not comparable to that of one who puts out only two quarts a day. The titer of urine in pregnancy is based on that per 1000 c. c. Aschheim and Zondek, who first did this in 1927, said normal pregnancy had a total of 50,000 units per liter. The highest titer of normal pregnancy is at the eighth week and may go to 150,000 units per liter. You must consider the specific gravity as well as the amount of urine; therefore, it should be calculated on a 24-hour specimen of urine. If the urine is to be shipped away, it should be sent away under a preservative. Urine should never be boiled, because boiling over 60° C. will destroy the hormone. I usually limit the patients to 400 c. c. of fluid prior to the collection of the first morning specimen.

I would like to remind you that many patients will give false positives from such factors as high increased intracranial pressure, tumors of the adrenal, tumors of the pituitary. These are isolated cases, however, but must be kept in mind. The urologist will also tell you that the cured case of teratoma of the testes will have more than 200 mouse units per liter of urine. That is not conclusive in all cases. Another point is the following of the case of hydatid mole. As I just mentioned, at the eighth week of pregnancy, the titer of urine may be 150,000 units per liter. Hydatid mole will give a high titer. Zondek, in 1927, brought out the fact that when there is hydatid mole or chorionepithelioma there will be a high titer. We did not get a positive Aschheim Zondek or Friedman modification in either of those cases proved hydatiform mole.

While this is the most valuable adjuvant, never let any laboratory test overrule your clinical judgment. If there is bleeding, whether the Aschheim-Zondek is positive or negative, empty the uterus.

May I warn you that you must follow the case of hydatiform mole for two years at intervals of two months, taking successive Friedman tests before you can tell the patient if she is cured, because there have been patients who, as long as eight to ten months later, developed chorionepithelioma when the Friedman test was negative in the interval. It is extremely valuable as a laboratory test, but do not overlook the fact that twin pregnancy and in hyperemesis gravidarum long associated, that there is concentrated urine which will give a high titer. I would be cautious about emptying the uterus unless there is bleeding because that may be twin pregnancy, for there are normal cases evacuated thinking hydatiform mole to be present.

Dr. A. V. Friedrichs (In closing): Concerning the question of the time factor regarding the opening of the rabbits brought out by Dr. King, I would like to state that when this test was originally started there was the concensus by all laboratory workers to open these animals in 24 hours after inoculation. We used that procedure but found that in one or two instances we were obtaining erroneous results because upon re-opening these animals at the end of 48 to 72 hours, a positive result would be obtained, whereas at the end of 24 hours a negative result was found. At the present time, unless there is a question of ectopic pregnancy, we do not touch these animals for 72 hours.

THE DIAGNOSIS AND TREATMENT OF STERILITY*

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This paper which includes a resumé of the important literature during the past two years is not being presented with the idea of bringing forth any original subject matter or for the purpose of adding any case histories or series to the already large accumulation, but it is being presented in an attempt to clarify some of that which has already been published. Within recent years there has been a steady advance in our knowledge of the many causes of sterile marriages and a corresponding advance in the effective and successful management of sterility. This knowledge to a large extent has penetrated the lay mind, and women who find themselves unable to reproduce present themselves to the physician fully expecting to obtain relief or satisfactory explanation for their plight.

It has been variously estimated that from 10 to 15 per cent of all marriages are sterile, that is, unable to achieve a pregnancy and a larger per cent if one includes women who abort habitually or whose fetuses regularly die *in utero* at or near term, though the latter two conditions cannot be considered as actual sterility. But, since the patient presents herself for the purpose of bearing a normal, living infant, these points deserve some consideration. Coupled with the above factors, when one considers the psychologic aspects of the problem and that one out of every ten women who consult the gynecologist does so because of the problem of sterility, its importance is immediately apparent.

The writer knows of no condition in which greater cooperation is offered by the female, but the male is often difficult to deal with because of his self-assured, procreative ability. It is here that the first and most important step should be taken, that is, an explanation to husband and wife of the complicated nature of sterility and that certain systematic and routine studies must be carried out in order to discover and treat as many as possible of the several causes in both sexes. Unless this is thoroughly agreed upon, it is best to explain that it is useless to begin. Mazer has, I believe, ably stated that such an investigation may take no less than eight months to one year because it is not well to discover one or two outstanding factors and be satisfied that these are the answer but to continue the investigation until the possible factors are eliminated, there now being recognized more than forty causes.

Many authors advise that since 25 to 50 per cent (average about one-third) of the cases are due to the male, he should be eliminated first. Since there are usually multiple factors in both sexes, this seems to be time consuming and to me a better plan would be to parallel the investigation in both so that each factor could be weighed separately and correlated with the others. Titus, in his new book on "Management of Obstetric Difficulties," offers a formidable plan of approach as follows: (1) History and general physical examination of husband and wife, including blood count and urinalysis; (2) pelvic examination of wife and examination of husband's genital organs; (3) estimation of basal metabolic rates of husband and wife; (4) postcoital examination of semen from a jar specimen and one from the cervical canal (Huhner test); (5) tests for tubal patency by air insufflation with atropine (Rubin test); (6) x-ray of uterus and tubes with opaque media; (7) hormone determinations of blood and urine; (8) endometrial biopsy. He states that with the exception of x-ray, visualization of the tubes and the laboratory estimations of the hormone values, the minimum requirements of a sterility study are that all of these steps must be carried out.

HISTORY

That the age factor is of importance is an obvious fact though some have attempted to prove that fertility exists in the

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male up to eighty years and beyond. To me, such cases are to be regarded with extreme suspicion. Female fertility has been shown to be greatest between ages 25 and 30 and male fertility between 25 and 35. The length of marriage has some bearing and nearly all are agreed that for all practical purposes three years of married life would seem to be an adequate length of time for conception to have occurred in normal persons. Low fertility of parents and close relatives may suggest some inherent glandular dysfunction. The history of previous marriages and pregnancies are obviously important. The one child marriage suggests the occurrence of pelvic disease following delivery, though all know that every individual has periods of greater and lesser fertility; diet, chronic illness, and so on, playing their parts. Mumps or scarlet fever may have rendered either partner sterile by involving the gonads; likewise, gonorrhea by its blockage of the various ducts in either sex. Pelvic peritonitis may have occluded the tubes by kinks and adhesions. Habits of intercourse may include innocuous lubricants or coitus interruptus with its resultant chronic pelvic congestion and tubal occlusion. Excessive intercourse may exhaust the male store of sperm. Dyspareunia is a subject in itself and must be managed accordingly. Previous operations, excessive use of alcohol, narcotics, possibly tobacco, lead poisoning, focal infections, chronic intestinal stasis, and excessive exposure to x-ray may be factors all worthy of consideration for obvious reasons. Sleep, rest, and exercise are important.

The importance of the menstrual history is immediately apparent when one considers that a history of irregular bleeding occurs in approximately 40 per cent of cases (Sheldon), and that rarely does a pregnancy occur in cycles under 27 days (Campbell). The age of onset of menses, periodicity of flow and the approximate amount of blood loss may give definite clue to endocrine dysfunction. Dysmenorrhea and clots are more suggestive of local disorders. Intermenstrual pain and/or bleeding may indicate ovulation.

EXAMINATION

In the examination of these patients, in addition to the thorough general checkup, it is important that a definite estimation of the endocrine status be made in both sexes, because there may exist such a degree of endocrinopathy that pregnancy would be contraindicated because of the likelihood of abnormalities in the offspring. Such an endocrine status may be determined from the height, weight, hair distribution, fat distribution, breasts, anthropometry and the basal metabolism. Thus, precocity is usually found in the low, fat, squatty, low metabolic girl. Delayed puberty, sterility and hypogonadism are usually found in the tall slender girl who exhibits underdevelopment of the breasts and genitalia and a height shorter than the armstretch or a measurement from the symphysis to the heel, longer than that from the symphysis to the vertex.

About two-thirds of all cases of so-called sterility in the female display some type of lesion in the pelvis, therefore this part of the examination must be done in absolute detail. Lesions of the vulva are rarely a cause of sterility but lacerations of the perineum favor the escape of semen from the vagina and may be responsible for secondary sterility. Congenital lesions must be appropriately managed. Inflammatory lesions of the vagina, particularly of the yeast and trichomonas varieties or in combination with *Streptococcus subaciditus* must be cured.

Sheldon states that 36 per cent of his series showed some lesions about the cervix. Erosions and ulcerations must be carefully cauterized, strictures dilated and cysts and polyps removed. The pH of the cervical secretions should be alkaline and if acid, indicate a pathologic disorder in the canal or higher in the generative tract.

The examination should next include a determination of the position, size, shape, and mobility of the uterus. Malpositions and fibroid tumors do not necessarily prevent but frequently hinder conception. Pal-

patory evidence of tubal disease should be sought; Kirtley found non-patent tubes in 50 per cent of his cases. The ovaries should be examined for size, position, fixation and possible evidence of ovulation. Ovarian cysts are not incompatible with conception but sterility is the rule.

For obvious reasons, routine as well as special laboratory work should be carried out on both sexes. The urine may reveal the presence of a previously undiscovered chronic nephritis. The stool may reveal any intestinal parasite common to the locality. Anemia, unless grave, is usually not regarded as an important factor but should be corrected. Litzenberg found hypothyroidism to be a major factor in 15 per cent of a large series. Since the basal metabolic rate is often misleading in borderline cases, it might be wise to consider thyroid medication as an empiric measure in all patients with a low plus level and below who can tolerate the drug without untoward symptoms.

In the oft encountered case wherein the male refuses to cooperate, the Huhner test has a bit to offer. The female is instructed to report within one hour after intercourse and without voiding as this may force the ejaculate from the vagina. If the vaginal pool and cervical secretions reveal a great number of actively motile spermatozoa, at least 75 per cent of which have normal morphology, it can be assumed with a fair degree of certainty that the male is capable of fertilizing his partner, and that the cervical secretions are not inimical to the sperm. Some investigators have claimed good results in male patients with abnormal number and mobility of sperm by the use of anterior pituitary and anterior pituitary-like hormones. Sufficient confirmation is yet lacking but these preparations should be given the benefit of the doubt in indicated cases.

Endometrial biopsy, best taken during the first eight hours of menstruation because of the possibility of disturbing an unsuspected pregnancy, is an extremely valuable and simple procedure. The investigator should familiarize himself with the various histologic patterns of endometria because, thereby, he can best correlate those findings with the clinical picture presented by the patient. This test, when abnormalities are found, is a definite aid in management of the case. Of greatest importance, it reveals the degree of ovarian efficiency. DeLee, in discussing pseudomenstruation as a cause of sterility in adult women states: "The exact frequency of anovulatory menstruation is unknown. Rock, Bartlett and Matson found the incidence to be 9.1 per cent in their sterility cases, whereas Effkemann found it to be 14 per cent. However, it is certain that anovulatory menstruation occurs much more often in sterile women than in women who have borne children. It must be remembered that anovulatory menstruation is not necessarily a permanent condition. Women may have ovulatory menses at times and anovulatory cyclic bleeding at others. Clinically the two are usually indistinguishable, but a study of the endometrium at the different times will reveal a secretory (normal early menstruation endometrium) phase during the periods of ovulation and a persistent proliferative (post-menstrual endometrium) phase during the periods of anovulatory menstruation." Though this has recently been questioned by Hamblin and others, it often gives indispensable information as to when and how hormone therapy should be instituted. It may be stated here that pregnant mare sera have not proved effective in the production of ovulation in women and monkeys (Ross) and should be discarded from the armamentarium in the treatment of sterility.

Novak believes that the riddle of ovulation is locked up in the pituitary gland and that a failure of ovulation is due to pituitary dysfunction, the luteinization mechanism not being touched off for some reason, thought to be caused by an imbalance between the anterior pituitary and the follicle. The unruptured follicle continues to grow and produces excessive amounts of estrogenic hormone until a reverse action is exerted on the pituitary and a resultant

check in the growth of the follicle which brings about a so-called withdrawal bleeding without ovulation.

In such cases, Hamblin suggests the utilization of "rest-periods" for the ovary by administering substitutional hormone therapy, in which, otherwise, withdrawal bleeding might be expected to occur, that is, estrogenic hormone throughout the intermenstrual period (this now being known to be secreted throughout the cycle) and luteinizing hormone during the latter half of the intermenstrual period. This process is continued for about four months after which a period of four months is allowed to elapse without therapy and the process is repeated. During the second or third series of therapy, anterior pituitary hormone may be added. The dosage of all is usually large but will not be discussed here because both the estrogenic and the luteinizing products in synthetic form for oral use soon will be on the market.

Obviously, the quantitative estimations of hormones in the blood and urine are important aids in the diagnosis and treatment of sterility but have the disadvantage of necessitating a well equipped laboratory and a trained technician. Thus far, sufficient data have not been compiled to rely too greatly on these findings but, suffice it to say, low values of the hormones in the blood or of their end products in the urine, when correlated with the other findings are indications for the administration of the corresponding products. These tests are also of diagnostic aid in determining the presence or absence of ovulation.

THERAPEUTIC AND DIAGNOSTIC AIDS

Aside from the general studies of the female, the Rubin insufflation test probably affords the greatest therapeutic and diagnostic aid in modern use. Ferguson claims that of 98 patients with patent tubes, 84, or 85.7 per cent, were known to have become pregnant following its use. In addition to its value in determining the patency of the tubes and after overcoming partial blockage, when combined with hysterosalpingography, it gives important information pertaining to the relationship which the fimbriated end of the tubes bears to the ovary, the position of the latter having been determined by bimanual palpation.

The test is performed preferably at least two days after completion of the menstrual period in order to prevent any possibility of backflow of endometrial tissue and at or just before the beginning of the conception period. The test may be repeated each month as this often temporarily overcomes a partial blockage. In cases which reveal a complete blockage, the test should be repeated with the patient under at least a moderate amount of sedation and atropine in order to overcome any tubal spasm which may account for blockage. The pressure should never be forced above 200 mm. of mercury for fear of rupturing an already damaged tube.

In cases which reveal some anatomic defect in the male such as hypospadias or some unusual condition in the female, mechanically preventing the spermatozoa from being deposited in the external os as revealed by the Huhner test, artificial insemination may be a solution to the problem though it is credited by the laity with being of much more value than it actually is. When this procedure is used, it must be accomplished with the least possible trauma, preferably with a flexible cannula, because any bleeding excited in manipulation will render the spermatozoon inert. One-half to one c.c. of the seminal fluid is sufficient in amount, the injection of a greater amount often being accompanied by intense cramp-like pain.

Of diagnostic aid in the management of any case of female sterility, the determination of ovulation is extremely important. Nearly every practitioner in gynecology has had the experience of feeling a small ovarian cyst rupture under the examining finger. Though this is not an oft encountered occurrence, it is of definite aid when correlated with the menstrual history. As stated above, endometrial biopsy probably is the greatest single aid in diagnosis of ovulation or anovulation. Novak, Hamblin and others have aptly stated that this test is not to be greatly relied upon because

the riddle of ovulation is still locked up in the pituitary gland. Zuck maintains that basal body metabolism as indicated by temperature recordings and basal metabolic determinations is a guide to the period of ovulation, a definite rise in these indicating that ovulation has taken place. Collins claims this to have been of little or no value in his hands. Hormonal studies will be dismissed by stating that their value in determining the occurrence of ovulation is unquestioned but have not yet become practical for general use because of the markedly technical nature of such tests. The examiner should use every facility at his command and if he be located at or near a well equipped medical center, all of the above methods may be utilized.

As DeLee suggests, it would be interesting and helpful to try to correlate Rubenstein's contention of a massive desquamation of the vaginal epithelium with a sharp rise in temperature, Zuck's claim of changes in the basal metabolic rate and temperature, the electric potentiometric method of Burr, endometrial biopsy, hormonal studies of the urine, and manual palpation when possible. With these and the aforementioned factors, we would then almost certainly arrive at a conclusion as to when ovulation occurred in a given menstrual cycle, even though some women ovulate and conceive during actual menstrual bleeding.

The occurrence of spontaneous abortion following therapy in cases of sterility is so common that these couples should be warned about this possibility. Since the advent of wheat germ oil and progesterone in the treatment of habitual abortion, there has been marked success in the management of same and it is therefore logical to advise that these drugs be used in these cases who become pregnant. Therapy is begun as soon as the pregnancy is suspected. Progesterone, one unit once a week, is given until the beginning of the fifth lunar month and wheat germ oil, thirty drops three times a day, is given until the beginning of the ninth lunar month or beyond.

Kaplan claims to have reestablished menstruation in 124 of 142 patients with amenorrhea and 52 of these subsequently become pregnant following roentgen ray therapy to the ovaries and pituitary and in a few instances to the thyroid. Mazer and Baer also bear out this contention as a therapeutic aid.

PRECAUTIONS IN DIAGNOSIS AND PROGNOSIS

Titus quotes Rubin as follows, "It is well to emphasize the fact that no couple should be told they are sterile unless all the factors have been most scrupulously analyzed and the examinations made with the greatest of care have corroborated each other and have been counterchecked."

It is distinctly wise to avoid a final verdict of hopeless sterility in any instance because of the untold harm which can obviously result in the psychic and family life of the couple in question and especially far reaching is the harmful effect upon the male. In cases of hopeless prognosis, the couple should be told that conception is uncertain and even unlikely under present conditions. Such advice often keeps the examiner from being caught "holding the bag", if an error is made and pregnancy does occur.

According to the extent of the desire of the couple for children, operative intervention may be resorted to in cases where possible aid may be obtained from such procedures as indicated, though remunerations for such efforts are few and far between.

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DISCUSSION

Dr. Conrad G. Collins (New Orleans): Now, about the definition of sterility: For years we have gone along with the definition that the woman should try at least three years to become pregnant, and if at the end of three years she had not become pregnant, that could be termed sterility. I believe that was all right years ago. I think we must modify the definition now, and that will answer Dr. Dial's couples who use contraceptives. Today, when families are planned as to number and when the pregnancy will take place, I think if the couples do not use contraceptives and desire a child, let them go four or five months without treatment. If not pregnant, I believe an investigation should be started immediately, and any factor that helps them become pregnant should be used.

As to whether contraceptives do or do not play a part in sterility, I am not certain. Some people insist that the use of contraceptives does decrease the fertility of the partners; I am not fully convinced of that myself.

You have heard Dr. Dial's reference to the case reported by Dr. King where the woman had an imperforate hymen, not infrequently this is a feature in sterility, and then the semen should be introduced into the uterine fundus, but there are uteri acutely anteflexed, where the cervix is against the anterior vaginal wall, where the cervix is displaced. There it is a good idea for the husband to introduce the penis into the vagina until the glans only is in the canal and let the ejaculate strike against the cervix. The use of that method will lower the number of operations performed for retrodisplacements in the treatment of sterility.

Another factor, especially when there is dyspareunia, is the amount of relaxation. We know ovulation takes place, in a 28 day cycle, on the tenth to fourteenth day. At that time, patients who are sterile, with a woman of the nervous type, no factor found, I prescribe a dose of sedatives such as nembutal or luminal prior to intercourse, to relax completely. Women, especially those who have relaxation, rectoceles, cystoceles, beginning prolapse of the uterus, quite frequently get up to urinate after intercourse and the semen runs out the vagina. Patients should be instructed that they elevate the hips on pillows following intercourse.

As regards ovulation, there are methods of determining when ovulation takes place. That, however, takes just an endometrial biopsy to prove that ovulation is taking place. We find one of two types of endometrium; either the proliferative stage, or the differentiating stage, which always means corpus luteum. As to time of ovulation, that can be determined electrically, but New Haven is the only place they have a vaginometer. The other method will be palpation of the woman's abdomen repeatedly throughout the menstrual cycle to see whether she is getting enlargement of one or the other ovary. Another method, introduced by Zuck, the accuracy of which is indefinite as yet, is taking the rectal temperature daily. He states that at ovulation time there is a drop of ½ degree. Certainly, there is no harm in doing that and if the patient has a decided drop, prescribe intercourse at that time.

Another factor is infrequently the patient has abdominal pain when she ovulates, in one side or the other, the "mittelschmerz" of the Germans, and will refuse to accept a partner at that time. It is just the time when she should have intercourse. If the pain is too great, prescribe codeine and let the patient have intercourse at the time she has pain.

As to dilatation of the cervix when the tubes are patent, about the tenth day of the cycle (the first day of the flow being the first day of the cycle) it is all right to dilate the cervix and insufflate the tubes, and frequently your efforts will be rewarded.

Hormones: To date I cannot say that any woman I have treated who has become pregnant has become pregnant as the result of estrogen, progestin, or pregnant mare serum. Those that have become pregnant have become pregnant by the use of thyroid extract and acceleration of the basal metabolic rate, whether normal or low. I believe it is the best endocrine product known today.

Wheat germ oil is valuable in keeping the pregnancy in the uterus, but I have seen no effect on

fertility as a result of the administration of wheat germ oil.

Surgery may be resorted to when patients need treatment of cervicitis or of fibroids. One word about tubal reconstruction; if you are going to reconstruct a patient's tubes that are blocked, remind her that she has one chance in 22 of ever delivering a full term viable fetus as a result of the operation.

Dr. Eugene H. Countiss (New Orleans): As to the use of iodized substances, I might mention a patient who was recently operated upon seven years after a salpingogram had been done with lipiodol. She had a suspension prior to the use of this oil and the tubes were then patent. In the absence of a history of infection, we felt justified in accrediting partially blocked tubes, perisalpingitis and oophoritis to the iodized oil. In another case, oil was found encapsulated within the fallopian tube six years after instillation.

I feel that it is rarely, if ever, necessary to instill opaque media at the time of tubal insufflation. A partially blocked tube may be completely occluded by the irritation of an opaque substance. As long as one tube is open to air, there is no necessity of salpingography, though if one is to be used, skiodan, which is more readily absorbed, is preferable.

Following an insufflation, a patient should never be told that the fallopian tubes are blocked unless the procedure is repeated at least once. Not infrequently tubes that are apparently closed to air injected through the cervix are found to be patent when insufflated from the fimbriated ends.

Dr. W. A. Dial (In closing): Obviously, the subject of sterility is so broad that all of its phases cannot be even touched upon in such a limited time.

Dr. Collins stressed the use of thyroid substance. There is no doubt that it is the most important hormonal drug used, not only in the treatment of sterility but also in the management of other gynecologic problems as well. It should be used as an empiric measure in all patients, both male and female, to the point of tolerance. Some may not tolerate more than 1/10 grain to start but they may be gradually worked up to tolerance and then the dose is slightly reduced and maintained.

As to the use of estrogenic and luteinizing hormones, we are not giving them in adequate dosage now. I believe that in a few months, those drugs will be available in new, oral forms and they will be a great deal more valuable than those which are used today.

Hamblin, who spoke here some months ago, stated that about 50 per cent of his cases are hormonal in origin but, remember, these are filtered cases; all of the minor problems have been ironed out before the patient is referred to him. He believes that the ovary, like any other tissue in the body, becomes overtaxed; it is working at full speed and this is not enough. He institutes rest periods by giving substitutional hormone as previously described. Novak, Hamblin, Ross, Collins and others claim that there have not been enough pregnancies following the use of pregnant mare's serum to warrant any further consideration of its use.

As Dr. Countiss stressed, I like to insufflate these patients each month prior to the conception period. If an unsuspected pregnancy already exists, it will not be disturbed by this procedure.

THE USE OF SULFANILAMIDE IN PERITONITIS*

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Peritonitis, whether it be localized or generalized, is still an important surgical problem. The mortality, in spite of many advances in treatment, remains appallingly high.

Since the introduction of sulfanilamide and related compounds, many types of surgical infections have been successfully treated with these drugs. One of the first experimental investigations demonstrating the value of sulfanilamide in hemolytic streptococcal infections was performed by Domagk[1] in controlling experimental mouse peritonitis. However, it has been only recently that the successful clinical use of the drug in peritonitis has been reported.

It is now the opinion of many clinicians that the use of sulfanilamide in adequate dosage is of definite value in the treatment of peritonitis. This opinion is based not only on recent reports of the actual successful use of the drug with an apparent improvement in mortality statistics, but also is based on well-known concepts of the pathology and bacteriology of peritonitis and the proved action of the drug on certain specific bacteria.

BASIC PRINCIPLES OF THE USE OF SULFANILAMIDE IN PERITONITIS

Chemotherapy, in any particular infection, should be based first of all on the effect of the drug on the specific bacteria responsible for the infection. Another fac-

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tor to be considered is the manner in which the drug is absorbed, distributed throughout the body tissues, and excreted. Furthermore, the actual pathologic changes which are present are also of importance in determining the effectiveness of the drug.

The use of sulfanilamide and allied compounds in the treatment of peritonitis is based on three principles: (1) The clinical and experimental evidence showing that the drug can be recovered in high concentrations in the peritoneal cavity; (2) the specific therapeutic effect of sulfanilamide on the bacteria most frequently found in cases of peritonitis; (3) the nature of the pathologic changes which take place in peritonitis.

Marshall,[2] Long,[3] and Bliss[3] have demonstrated that sulfanilamide diffuses rapidly into all body tissues and fluids. Furthermore, the drug is present in relatively high concentrations in the peritoneal fluids. Long[3] and Bliss[3] have also demonstrated the presence of sulfanilamide in transudates and exudates.

Ravdin, Rhoads, and Lockwood[4] have shown in experimental animals that the sulfanilamide concentration in the peritoneal fluid reaches a high level in as short a time as an hour and a half after the administration of sulfanilamide by hypodermoclysis. It is therefore evident that sulfanilamide is present in the normal fluid of the peritoneal cavity, as well as in the pathologic exudates and transudates. This is now considered to be true of all the serous membranes of the body, and is the basis of the treatment of arthritis, meningitis, and empyema, as well as peritonitis.

The specific effect which sulfanilamide has on certain particular micro-organisms is important in explaining why sulfanilamide should be of value in the treatment of many types of peritonitis.

The most frequent type of peritonitis with which we are obliged to cope is that type occurring as a complication of appendicitis, with or without actual perforation. In this condition, it is generally accepted that the colon group (*B. Coli* and others) and streptococci are the most common invaders of the peritoneum.

Experimentally, Bower, Burns, and Mengle[5] have produced appendiceal peritonitis by ligating the base as well as the blood supply in dogs, followed with a large dose of castor oil. In the resulting peritonitis in these animals, the colon group and streptococci were the most frequent organisms isolated.

Ravdin,[4] in a large series of peritoneal cultures in appendiceal peritonitis, found *B. coli* to be the most frequent organism cultured. Streptococci, both hemolytic and non-hemolytic, were next in frequency. Corry, Brewer, and Nicol[6] and others report similar results in their investigations of the bacteriology of appendiceal peritonitis.

Long,[3] Bliss,[3] Domagk,[1] Lockwood[7] and numerous other investigators have proved conclusively, both experimentally and clinically, that sulfanilamide is of definite therapeutic value in the treatment of infections due to many types of streptococci, both hemolytic and non-hemolytic.

The efficiency of sulfanilamide against *B. coli* is almost as widely accepted. Burns[8] states that over 60 per cent of urinary tract infections due to *B. coli* can be cured with sulfanilamide. Cokkinis,[9] Helmholz,[10] and others also report the efficacy of sulfanilamide in the treatment of urinary infections due to the colon group. It is reasonable to believe that sulfanilamide would also be effective against colon infections of the peritoneal cavity.

The importance of anerobes in appendiceal peritonitis has been stressed by Bower,[5] Ravdin,[4] and others. *Clostridium welchii* is the most frequent anerobe that can be cultured. When anerobes can be isolated by cultures from the peritoneum, *B. welchii* is found in over 60 per cent of the cases according to the statistics of Bower, Burns, and Mengle.[8] Bohlman[11] and others have demonstrated the chemotherapeutic value of sulfanilamide in infections due to *B. welchii*. Therefore, it is evident that sulfanilamide has a specific action against the colon group, streptococci, and *B. welchii*,

the three most common organisms isolated in appendiceal peritonitis.

It is probably true, also, that these are the principal micro-organisms involved in perforation of the large and small bowel at other points, with resulting peritonitis.

Cheney,[14] and Walters[15] have shown that the colon group of organisms as well as streptococci are also the most frequent micro-organisms involved in cholecystic disease. Cokkinis[9] has reported good results in the conservative treatment of acute cholecystitis with sulfanilamide, and it is reasonable to assume that the drug would also be of value in those cases complicated by peritoneal involvement.

Practically all authorities agree that sulfanilamide has a specific action against infections caused by the gonococcus. In pelvic peritonitis as a complication of gonorrheal disease of the female generative organs, the most frequent secondary invaders are streptococci and the colon group. Therefore, from a bacteriologic standpoint, sulfanilamide should be of value in such cases.

In peritonitis resulting from puerperal sepsis or other obstetric complications, streptococci are the offending micro-organisms in a large percentage of the cases. It is generally agreed that sulfanilamide is highly effective against such infections.

In so-called primary peritonitis, that type in which no definite intra-abdominal focus is present and which is considered to be blood borne, sulfanilamide is of value in a large percentage of cases. This type of peritonitis occurs practically always in children. In an analysis of 67 cases, Ladd, Botsford, and Curnen[16] have shown that 47 cases (70 per cent) were due to streptococci. In these cases, caused by the streptococcus, large doses of sulfanilamide are of definite value. In the remaining 30 per cent of these cases of primary peritonitis, the pneumococcus was the offending organism. Sulfapyridine therapy is indicated instead of sulfanilamide.

The importance of making a bacteriologic diagnosis either by blood culture, or by parencentesis and culture of the fluid obtained, or by cultures from the peritoneum at operation, is extremely important in the handling of cases of childhood primary peritonitis. Chemotherapeutic measures with sulfanilamide and sulfapyridine, as well as specific pneumococcal serum, give a much more hopeful outlook in such cases.

In summarizing this brief review of the bacteriology of peritonitis, it is evident that many types of peritonitis are caused by micro-organisms which are susceptible to sulfanilamide and allied compounds.

Lockwood, Coburn, and Stokinger[7] believe that the gross pathologic characteristics of any particular infectious lesion are of importance in determining the effectiveness of sulfanilamide in the treatment of the condition. It is their opinion that any infection, which is characterized by rapid invasion of contiguous structures, and associated with a minimal degree of necrosis, responds more favorably to sulfanilamide than an infection in which there is considerable tissue injury and necrosis, or which is confined to a localized abscess. This is borne out clinically by the fact that septicemia,erysipelas, septic sore throat, puerperal sepsis, lymphangitis, meningitis, as well as peritonitis and other conditions of the former type, respond well to sulfanilamide, whereas localized abscesses, of all types, infected hematomas, chronic osteomyelitis, and similar conditions, respond very poorly if at all.

Snodgrass[17] explains the efficacy of sulfanilamide against streptococci on the grounds that "invasiveness" is the most outstanding characteristic of this organism from a standpoint of pathologic physiology. It is against this property of "invasiveness" that sulfanilamide is most valuable, be it a streptococcus or any of the other micro-organisms successfully combated by the drug.

Peritonitis is definitely a type of infection characterized by rapid spread. The peritoneum is richly supplied with blood vessels and lymphatics, and seldom do we see ulceration or gangrene, although localized abscesses do occur.

The importance of the blood supply to an organ or tissue is another factor in determining the effectiveness of sulfanilamide. The drug is distributed through the blood stream, and diffuses out into the body tissues. Thus, the rich vascularity of the peri-

toneum, particularly in inflammatory conditions, is an important factor in the effectiveness of sulfanilamide in peritonitis.

RESULTS OF TREATMENT

A number of favorable reports have recently been made on the actual treatment of peritonitis with sulfanilamide and related compounds. Most of these reports are concerning the successful treatment of appendiceal peritonitis.

From an experimental standpoint, Bower, Burns, and Mengle[5] have produced appendiceal peritonitis in dogs as mentioned above. In a control series, in which the usual methods of treatment were used (without sulfanilamide), the mortality was 91.7 per cent. In another group of animals receiving the same type of treatment in addition to sulfanilamide, the resulting mortality was only 50 per cent.

Ravdin,[4] in treating a large series of cases of acute appendicitis, with and without peritonitis, has reduced his mortality from 1.5 to 0.4 per cent in all cases of acute appendicitis. The use of sulfanilamide was the only change in his method, and was used only in those cases with actual complications or threatened complications. Cokkinis,[9] Corry and Brewer,[6] Nicol,[6] and others have also reported the value of sulfanilamide in the treatment of appendiceal peritonitis.

Ladd, Botsford, and Curnen,[16] and Banks[18] have reported favorable results in the treatment of primary streptococcal peritonitis with sulfanilamide. These same writers report the successful treatment of primary pneumococcal peritonitis with sulfapyridine.

There are only isolated instances in the literature dealing with the successful treatment of peritonitis due to cholecystic disease, or other perforations of the intestinal tract. However, as previously stated, because of the pathologic picture in these types of peritonitis and because of the type of bacteria usually isolated, sulfanilamide therapy should be of value.

SUMMARY OF TREATMENT OF 14 CASES OF PERITONITIS

During the past four months, on the Surgical Service at Touro Infirmary, 15 patients with various types of peritonitis have been treated with large doses of sulfanilamide given subcutaneously as a hypodermoclysis. This series is far too small to justify any final conclusions as to the value of sulfanilamide in peritonitis. Nevertheless, the fact remains that all of these were extremely ill patients, classified definitely as peritonitis of various types, and there has been no mortality. Furthermore, there have been no serious toxic effects from the administration of large doses of sulfanilamide by hypodermoclysis of these cases. Ten of these 15 cases are classified as appendiceal peritonitis; four of the ten are classified as generalized peritonitis, and six as spreading peritonitis.

There were two cases of pelvic peritonitis resulting from septic puerperal complications. The remaining three cases were postoperative complications of a ruptured tubo-ovarian abscess, of an abdominal complete hysterectomy, and of a vaginal hysterectomy. All of these patients received large doses of sulfanilamide by hypodermoclysis, and all have recovered.

METHOD USED IN ADMINISTRATION OF SULFANILAMIDE

In treating these 15 cases, the technic recently advocated by Ravdin has been closely followed. A normal saline solution containing 120 grains of crystalline sulfanilamide to each 1000 c. c. is administered as a hypodermoclysis. The average adult usually received 250 c. c. of this solution every six hours, amounting to 1000 c. c. or 120 grains during 24 hours. This dose was either continued for several days or gradually reduced depending on the response of the patient. The hypodermoclyses were usually administered into the lateral aspect of the thighs, with no serious discomfort to the patient. In a few cases, only 90 grains per 24 hours were given to adults.

Children received smaller doses, depending on their weight and age. However, children, generally speaking, tolerate the drug better than do adults. Relatively higher

dosages are necessary in children to maintain an adequate blood concentration. This is probably due to the fact that the renal function of children is usually better than the average adult. Sulfanilamide, as is well known, is almost entirely excreted by the kidneys.

There are two phases concerning the administration of sulfanilamide to surgical cases which should be stressed. First, an adequate blood concentration should be maintained, that is, at least 5 mg. per 100 c. c. Secondly, the drug must be administered at regular hourly intervals so as to maintain the blood concentration at a constant level.

The average blood level in this series was 6.9 mg. The drug was administered regularly day and night at six hour intervals. The average duration of administration of the drug was four to four and half days, being discontinued when it was believed the infection was definitely under control.

Maes[19] states that he has previously used intramuscular injections of prontosil in the treatment of peritonitis. However, in spite of relatively large doses, he was not able to obtain blood sulfanilamide levels high enough to be of therapeutic value. For this reason, he also now advocates the use of the highly purified, soluble form of sulfanilamide known as "prontylin crystals," given in a hypodermoclysis of normal saline. By using the drug in this form, it is possible rapidly to obtain and maintain high blood concentrations.

The administration of sulfanilamide by hypodermoclysis in peritonitis is superior to mouth administration for a number of reasons. The absorption of the drug from the gastrointestinal tract is much slower and much less constant than when given by the parenteral route. Furthermore, the nausea, vomiting, and distention which so often are present in peritonitis make the administration of the drug by mouth particularly ineffective. Added to this is the nausea and vomiting which may be produced by the drug itself.

In primary pneumococcal peritonitis in children, sulfapyridine in the form of the soluble sodium salt can be administered in large doses either intravenously or by hypodermoclysis. I have had no recent experience with primary pneumococcal peritonitis, but have witnessed the successful administration of sulfapyridine to pneumonia patients both by the subcutaneous and intravenous routes.

TOXICITY

The toxic manifestations of sulfanilamide when administered by hypodermoclysis are essentially the same as those which occur when the drug is given by mouth. In this particular series, the toxic manifestations of the drug have been very mild, although relatively large doses have been given.

Cyanosis was the most frequent toxic manifestation. In 14 patients, nine had cyanosis of varying degrees. Long[3], Bliss[3], Ravdin[4], Snodgrass[17] and other authorities agree that this cyanosis is not to be regarded seriously. It is by no means an indication for stopping sulfanilamide therapy. In this series, the cyanosis was disregarded almost entirely unless accompanied by other more serious manifestations of drug toxemia.

Of these 14 patients, four showed a slight decrease in the red blood cell count, which may or may not have been due to the drug. In two instances there was a slight fall in the white blood cell count during the time sulfanilamide was administered. In none of these patients, however, was there a marked leukopenia, agranulocytosis, or anemia which could be definitely attributed to the drug. However, during the administration of sulfanilamide, the blood picture must be followed closely from day to day, because agranulocytosis and hemolytic anemia are two of the most feared toxic manifestations of the drug. A complete blood picture should be recorded every 24 to 48 hours during sulfanilamide therapy.

In practically all of these patients, there has been a definite tendency to an acidosis. This chemical imbalance was combated by the administration of Hartmann's solution intravenously. Other observers have also reported this phenome-

non, and have recommended the administration of sodium lactate intravenously or sodium bicarbonate by mouth as methods of combating the acidosis. Because of this disturbed chemistry, these patients should have frequent blood chemistry determinations.

Recently, at the New Orleans Graduate Medical Asembly, Braasch[20] of the Mayo Clinic, warned against use of sulfanilamide by hypodermoclysis because of the local tissue necrosis which may take place at the site of the injection. This has not been my experience. I have administered the highly purified form of sulfanilamide crystals by hypodermoclysis in over 30 cases of peritonitis and other conditions, without a single instance of local tissue damage. It is my opinion that this method is comparatively safe if the crystalline sulfanilamide is administered in a sterile saline solution at a reasonably slow rate and with strict aseptic precautions.

Although we have been fortunate in that there have been no serious toxic effects from the drug in this series of cases, the importance of the toxicity of sulfanilamide cannot be too strongly emphasized. Patients receiving large doses of sulfanilamide must be closely observed. The occurrence of fever out of proportion to the disease itself should frequently be a warning signal. According to Long and Bliss[3], this "drug fever" frequently precedes by several days the more serious toxic complications such as jaundice, hemolytic anemia, or agranulocytosis. As Cokkinis[9] has said, sulfanilamide is a "double edged weapon" and evidence of toxicity must be closely watched for. The drug should be stopped immediately if there is any indication that serious toxic effects may take place.

At the present time, sulfanilamide is widely used for many types of infections. It is frequently of value to question patients before beginning sulfanilamide, as to whether or not they have previously taken the drug. A history of intolerance to the drug is probably the only contraindication to trying its use in those infections where it is known to be of value.

OTHER PHASES OF THE TREATMENT OF PERITONITIS

In discussing the use of sulfanilamide in peritonitis, the other phases of the treatment of this serious surgical condition are not to be overlooked. My experiences with the Miller-Abbott tube in approximately 35 cases of paralytic ileus, both with and without peritonitis, have been extremely gratifying. This method of intestinal intubation is an important advance in the treatment of both mechanical and paralytic ileus. In this small series of 14 cases, the Miller-Abbott tube was used successfully in seven of the 14 cases.

Furthermore, the peritonitis case should receive adequate intravenous fluids and blood transfusions as indicated. Transfusions should probably be used more frequently when large doses of sulfanilamide are given, because of the tendency of the drug to cause a decrease in both the red and white blood cells. The chemical balance of the patient must be closely watched, and fluids administered accordingly. Vitamins are administered by the parenteral route as indicated. The patient, generally speaking, should receive practically nothing by mouth. Adequate sedation, particularly in the form of morphine, should be prescribed.

LOCALIZED PERITONEAL ABSCESSES

The use of sulfanilamide in peritonitis does not eliminate the necessity of frequently draining localized abscesses. In this series of 14 cases, six localized abscesses developed, all of which were successfully drained. All six of these occurred in patients with appendiceal peritonitis, three in the cul de sac, and three in the lower right quadrant.

Any patient with peritonitis who is receiving sulfanilamide therapy should be watched closely for the occurrence of abscesses. Sulfanilamide is not to be considered the treatment of choice in localized intraperitoneal abscesses. The correct treatment is still incision and drainage, if actual pus is present. Sulfanilamide, however, it is believed will tend to prevent a generalized spread of the infection.

Furthermore, localized palpable inflammatory masses of the peritoneum will frequently resolve under sulfanilamide therapy. Cokkinis[9] has reported excellent results in the delayed treatment of complicated appendicitis with a palpable inflammatory mass in the lower right quadrant. In a very large percentage of his cases, these masses resolved spontaneously under sulfanilamide therapy.

PROPHYLACTIC USE OF SULFANILAMIDE

The use of sulfanilamide in the prophylaxis of peritonitis in cases where contamination of the peritoneal cavity is expected merits further study. In a few isolated cases, the drug has been used pre- and postoperatively in operations upon the large bowel. These reports, however, are too few to justify any conclusions at the present time.

There is a conflict of opinions as to the exact effect of sulfanilamide on the antibody mechanism. Cokkinis[9], for example, states that the sulfanilamide should not be used in acute appendicitis during the first 48 hours, because the administration of the drug may interfere with the immunity response. On the same basis, the drug should possibly not be given in peritonitis cases until the infection has established itself and an immunologic response is manifest usually by the presence of fever and leukocytosis. Therefore, it is evident that the value of sulfanilamide as a prophylaxis against peritonitis is still uncertain.

SUMMARY

The use of sulfanilamide in peritonitis is based on three principles: (1) The presence of sulfanilamide in large concentrations in the fluids and exudates of the peritoneal cavity; (2) the specificity of sulfanilamide in combating the micro-organisms most frequently isolated in peritonitis; (3) the property of the drug to be more effective against lesions presenting the pathologic characteristics of rapid spread with little local reaction and necrosis such as is present in peritonitis.

Fourteen patients with peritonitis of various types who have been treated with large doses of sulfanilamide have been studied. There has been no mortality. This series is to small to draw any final conclusions; however, I believe the results justify this preliminary report.

The administration of crystalline sulfanilamide in saline solution, according to the technic recently advocated by Ravdin, is recommended as the method of choice in peritonitis. The drug is administered as a hypodermoclysis at regular hourly intervals. Doses of 120 grains per 24 hours are generally given to adults. It is recommended that the blood concentration be kept above 5 mg. until the infection is under control.

In this series, there have been no serious toxic reactions. However, the toxic effects of the drug are not to be underestimated, and must be carefully guarded against.

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I imagine almost all medical students pick out one or several men in their profession and try to duplicate their careers to a greater or lesser extent. However, few if any, at least in recent years, have attempted to follow the example of Dr. Thomas Hunt. And this is unfortunate, for that man was not only one of the best doctors in his part of the country, but also a great organizer. It was he who was largely responsible for establishing and building up what is known today as the Tulane University School of Medicine.

Dr. Thomas Hunt was born in Charleston, S. C. on May 18, 1808. He came from two very distinguished families, and he and his brothers carried the name to even greater glory. His paternal grandfather was Governor of Bahama and president of the King's Council at Nassau. His father, following more or less this same line, came to Charleston to establish his law practice. Here, he became a planter and a member of the Legislature of South Carolina, besides serving his original profession. Mr. Hunt married a woman of a distinguished South Carolina family, and had five children—all boys.

The life of young Thomas pointed strongly toward a legal career, as did his brothers'. However, in his late teens he deserted his family's profession and turned to the study of medicine. He attended the University of Pennsylvania and was graduated from this institution in 1829. He then returned to Charleston, but soon left to study at the great medical center of the world—Paris. He remained here for 18 months, but was then called home by the untimely death of his father. He now settled down to practice medicine in Charleston.

His first big opportunity presented itself when the brig Amelia was wrecked on Folly Island, just outside the harbor of Charleston. An epidemic of cholera broke out among the passengers of this ship, and Dr. Hunt was called upon for his services. He performed nobly, and worked untiringly until the epidemic was checked. However, the important part of this episode was that Dr. Warren Stone was a passenger of this ship, and a firm friendship was established that was to last for over 30 years.

In 1833 Hunt came to New Orleans to study cholera and established a fine reputation. He was soon elected surgeon to Charity Hospital, but relinquished this position because of its poor remuneration and because he had already formulated plans for establishing a medical school in New Orleans, and chose to devote his time to this undertaking.

Dr. Hunt worked unceasingly in organizing this school, and in 1834 the Medical College of Louisiana was founded. Dr. Hunt was made professor of anatomy and physiology and was elected dean.

It should be said that the new organization met a great deal of unexpected opposition in this city. Professional jealousy reared its ugly head, as a great many of the older doctors had not been invited to serve on the faculty. They united their efforts to break up the school, and this proved to be a serious affair since the prestige they enjoyed made them a powerful force in the city. Among the chief complaints was the fact that classes were conducted in English instead of French, and indeed, many of these men could not speak English. However, by the perseverance and hard work of the founders, the school opened and functioned successfully.

The records tell us that Dr. Hunt resigned from the institution in 1835, and although the exact reasons are unknown, it is stated that the resignation proceeded from "the most honorable and disinterested motives."

Until 1843 the medical college was financed through private enterprise, but now it received direct aid from the state. Although at this time Dr. Hunt was not officially connected with the school it is said

*Read before the Orleans Parish Medical Society, May 13, 1940.

†From the History of Medicine Society, Tulane University.

that he was instrumental in obtaining this state aid. He worked further along this same line and in 1845 a new state constitution was drawn up and a clause included to establish a state university with the medical college a part of this university. Dr. Hunt was largely responsible for this action as he sacrificed his private practice to devote his activities to make the school a permanent state institution.

The medical school was now well established, and in 1850 a medical museum was founded that was said to be equal to the best in the United States and Europe. The school continued to prosper until the War Between the States forced it to suspend its activities.

After the outbreak of the war, Dr. Hunt went to Havana, as his health was very poor; but he was not happy there, largely due to his difficulty with the language. He then went to Bermuda and remained there until the end of the war, when he returned to New Orleans.

On his return, he was elected President of the University of Louisiana and immediately set to work to restore its former prestige. However, he overtaxed himself, and his health finally gave way altogether. In 1866, he became a confirmed invalid, and finally died on March 20, 1867.

With regard to his medical career, it must be said that Dr. Thomas Hunt was looked upon as one of the ablest doctors of his time. He served as professor in the chairs of anatomy and physiology; pathologic anatomy and clinical practice; physiology and pathology; and special pathologic anatomy. He was also president of the Physico-Medical Society.

Dr. Hunt was not a prolific writer, and in fact published very few medical articles. However, he enjoyed a fine reputation as a lecturer, and was popular with both the students and his colleagues.

The outstanding achievement in the life of Thomas Hunt was to promote medical education here in the South, and through his great interest, untiring spirit, and ability to deal with and understand people, he accomplished his purpose nobly and should be remembered as a great educator, doctor, and man.

In concluding this brief resumé of Dr. Hunt's activities, I would like to read the inscription on the marble plaque which Tulane University has erected in memory and appreciation of the efforts of Dr. Thomas Hunt:

"The faculty of the medical department of the University of Louisiana have erected this tablet in memory of Thomas Hunt, M. D., a founder of the Medical College of Louisiana in September, A. D. 1834, who was born in Charleston, South Carolina, May 18, 1808, and died in this city March 20, 1867. He was then third president of the University of Louisiana and professor of physiology and pathology in the medical department. In the loss of Professor Hunt the University of Louisiana mourns its most gifted and eloquent teacher, the profession of medicine, an accomplished, elevating, and independent leader, and in science, an enthusiastic and untiring votary. He brought to his instruction in physiology the resources of a cultivated and learned experience and his demonstrations in pathological anatomy, repeated for years in Charity Hospital, conducted by a master imbued with a profound knowledge of the subject and remarkably graceful and skillful in the use of the knife, constituted a course the most perfect ever delivered on this continent. The services of Professor Hunt as the presiding and executive officer of this department, his valuable donations to it, and the large increase in the resources of the institution, obtained mainly by his energy and his influence from the representatives of the state, have entitled him to this grateful memorial."

NEW ORLEANS
Medical and Surgical Journal

Established 1844

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H. W. Kostmayer, M. D.
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1430 Tulane Avenue

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THE NEED FOR PHYSICIANS

Already the medical profession has felt the withdrawal from its ranks of many physicians who have been called into active service. Not only have doctors actually gone into the military services of the United States, but many of them who are still in civil life are doing much work for the Government on a purely voluntary basis. The medical personnel of the draft boards is an excellent example and probably makes up the largest group of physicians who are performing extra-military services. There are others, moreover, who have been called upon to help and aid in the defense program in other ways.

The medical profession is not only giving its services freely and willingly to the Government but there is a call for physicians for many activities which result from the speeding up in industry and the expenditures of large amounts of money. The demand for physicians, for the most part younger men who have not as yet been placed in their proper niche for life, is tremendous. There is need for younger doctors everywhere, but the supply at the present time does not seem to meet the demand.

It is earnestly hoped that the army will not call into active service any more medical men than are absolutely necessary. The life of the doctor who has been called into active service is in sharp contrast to the life he leads when he has the status of a civilian. He is not required to give many hours to his work, has much idle time and often the work two or three men are doing could be done by one without straining himself. It seems a great pity when there exists a heavy civilian demand for doctors that many a non-regular medical army officer is spending only a few hours a day in his actual professional duties. Most of the medical men do not need training unless they are going to serve directly with combat troops. Even then the training could and should be accomplished in a few months. The men who are serving in army hospitals will function very much as they do in civilian life; an orthopedic surgeon in an army hospital will do the same type of work that he would do in a private institution and so will the urologist, the surgeon, the internist or the head specialist. It is to be hoped most earnestly that the Surgeon General's office will not continue to call out more physicians than are needed unless there is an actual necessity for them. The army has asked the civilian doctors to cooperate; it is only fair that the doctors in civil life should likewise ask the army to cooperate in their problems.

INFLUENZA

The recent mild epidemic of influenza has apparently caused very much more disturbance in the minds of the laity than the actual severity and incidence of the disease would warrant. Of course it is obvious, that to the lay mind an epidemic of influenza implies a severe catastrophe such as occurred in 1918, consequently there has been a lot of unnecessary and needless worry. As a matter of fact the so-called epidemic has never reached epidemic proportions. It is true that there has been a considerable amount of sickness of a minor nature in the population of south Louisiana at least. This has been greatly exaggerated. In one of the current news weeklies from Alexandria, for example, it was reported there were 25,000 cases. Of course this is a gross overstatement. If the reported cases from New Orleans are any indication of the actual incidence of the disease, then influenza has been no more prevalent than it usually is at this time of the year. In most instances the expressions of the disease have been so minimal that the physicians of the state have not bothered to report any but the relatively severe cases.

Another feature of influenza that might be mentioned is that any respiratory tract infection, when there are a few cases of influenza in the neighborhood, is promptly labeled influenza. It is not only the respiratory tract infections, the common cold for example and the acute bronchitis of winter time that are dubbed influenza, but also any minor infection, be it systemic with a rise in temperature, is promptly accredited to influenza although it might be due to any one of a number or variety of micro-organisms, any one of which will produce atypical symptoms of the disease.

Influenza is a virus infection which is characterized by certain definite clinical expressions and which, without the concomitant superimposed streptococcic or bacterial invasion of the lung, will produce a few days of discomfort, miserableness and wretchedness in the patient but leaves no after effect of any moment. Extremely rare is a true virus pneumonia and in the present flare-up of the condition there have been few secondary pulmonary complications.

It might be well for physicians to stress the mildness of the present influenza and to ease the minds of their friends and patients by telling them that as it is now there is nothing about which to worry. An epidemic such as this might, in theory, be stopped if everyone could be segregated and separated from his fellowman. There is no such possibility. Merely the closing of the schools would accomplish nothing unless the children were kept from movies, churches and from playing together. These measures of course would be possible only in the event of an epidemic comparable to that which occurred twenty odd years ago.

THE TREATMENT OF EPILEPSY

In 1938 Merritt and Putnam[1] reported on the use of dilantin and sodium in the treatment of epilepsy. Their report was most interesting and resulted in the stimulation of many to employ this drug in the treatment of the epileptic patient. There have been half a dozen or more papers on this subject, all of which substantiated the original observation that dilantin is capable of reducing markedly the number of convulsive seizures that occur during the course of the day in the patient who has epilepsy. Many of these papers deal with the toxic effects of the drug as well as the improvement in the patient's general well being, alertness and personality. In order to demonstrate the value of this drug the most recent paper on the subject might be quoted. Ross and Jackson[2] studied 73 patients in the Caro, Michigan, State Hospital for Epileptics. To these patients they gave the drug in doses from 0.1 to 0.5 gram depending upon the number of seizures daily. Most of these people were young in age. The authors were particularly interested in studying the conduct of patients and what effect it had upon their alertness, initiative, behavior and cooperation. In analyzing results it might first be said that after an extended trial period of a year to a year and a half, it was noted in 65 per

cent of patients the incidence of the seizures was reduced 75 per cent or more. In approximately half of the patients there was definite improvement in conduct, notably in those patients whose seizures were markedly diminished. However, there are a certain number, in whom, in spite of the reduction in the number of attacks, there was no improvement in their conduct. The patients were divided into the usual classification and it was found that the drug did not materially affect the responsiveness in any one group of epileptics over another. It is to be noted, however, that there was not as great a degree of improvement in the number of attacks in the encephalitic group whereas in the epileptics and the traumatic group, only seven in number, the reduction in the number of attacks was greatest.

The use of dilantin and sodium is to be enthusiastically encouraged. It is a drug with few if any toxic effect, with the power of markedly reducing the number of seizures and with the result that in many instances there is an improvement in deportment, initiative, interest and willingness to cooperate. Epilepsy is a most unfortunate condition and it goes without saying that any medication which will improve the saddening effects of this disorder should be employed regularly.

1. Merritt, H. H., and Putnam, T. J.: Sodium diphenyl hydantoinate in the treatment of convulsive disorders, J. A. M. A., 111:1068, 1938.

2. Ross, A. T., and Jackson, V.: Dilantin sodium: its influence on conduct and on psychometric ratings of institutionalized epileptics, Ann. Int. Med., 14:770, 1940.

TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

CALENDAR

February 3. Orleans Parish Medical Society Board of Directors, 8 p. m.
Clinico-pathologic Conference, Hotel Dieu, 8:15 p. m.

February 4. Eye, Ear, Nose and Throat Hospital Staff, 8 p. m.

February 5. Clinico-pathologic Conference, Charity Hospital Morgue Amphitheater, 1:30 p. m.
Hutchinson Memorial Clinic Staff, 8 p. m.
Mercy Hospital Staff, 8 p. m.

February 6. Clinico-pathologic Conference, Touro Infirmary, 11:15 a. m. to 12:15 p. m.

February 10. Orleans Parish Medical Society, 8 p. m.

February 11. Eye, Ear, Nose and Throat Society, 8 p. m.

February 12. Clinico-pathologic Conference, Charity Hospital Morgue Amphitheater, 1:30 p. m.
Touro Infirmary Staff, 8 p. m.
Woman's Auxiliary, Orleans Club, 3 p. m.

February 17. Hotel Dieu Staff, 8 p. m.
Clinico-pathologic Conference, Baptist Hospital, 8 p. m.

February 18. Charity Hospital Medical Staff, 8 p. m.

February 19. Clinico-pathologic Conference, Charity Hospital Morgue Amphitheater, 1:30 p. m.
Charity Hospital Surgical Staff, 8 p. m.
The Orleans Tuberculosis Hospital Staff, 8 p. m.

February 20. Clinico-pathologic Conference, Touro Infirmary, 11:15 a. m. to 12:15 p. m.

February 21. I. C. R. R. Hospital Staff, 12 noon.
New Orleans Dispensary for Women and Children Staff, 8 p. m.

February 25. Baptist Hospital Staff, 8 p. m.

February 26. Clinico-pathologic Conference, Charity Hospital Morgue Amphitheater, 1:30 p. m.
French Hospital Staff, 8 p. m.

February 27. Clinico-pathologic Conference, Touro Infirmary, 11:15 a. m. to 12:15 p. m.

February 28. L. S. U. Faculty Club, 8 p. m.

The following program was presented at the regular scientific meeting of December:

1. Plasma Therapy
   By Drs. D. N. Silverman and R. A. Katz.
2. The Use of Plasma in Surgical Practice
   By Dr. Mims Gage

During the month of December one joint scientific meeting was held with the Charity Hospital Staff. The following program was presented:

1. Hematuria Complicating Pregnancy
   By Drs. E. L. King and John Menville
2. Spontaneous Mediastinal Emphysema
   By Dr. Edward Matthews
3. Marfan's Syndrome.....By Dr. Morris Shushan

4. Postoperative Atelectasis - Bronchoscopy
By Drs. Wolf, Fatter and Hays
5. Diagnostic Problem
By Drs. R. H. Turner and J. Magne

TREASURER'S REPORT

Bank Balance, November 30, 1940	$3,440.62
December Credits	1,731.32
Total Credits	$5,171.94
December Expenditures	1,470.71
Actual Book Balance, December 31, 1940	$3,701.23

During the month of December the Society had the misfortune of losing one of its active members, Dr. Frank J. Kinberger.

The following physicians were elected to membership in the Society during the month of December: Active: Drs. Robert A. Katz and John G. Pratt; Intern: Dr. Hardee Bethea.

NEWS ITEMS

At a recent meeting of the Central Psychiatric Society in Milwaukee, Dr. Gilbert C. Anderson was elected to membership.

Drs. Rena Crawford, Don Julian Graubarth and Suzanne Schaefer attended the annual national meeting of the American Academy of Pediatrics at Memphis. Dr. Graubarth served as secretary of the symposium on pneumonia.

Dr. John H. Musser recently attended the meeting of the sub-committee on medical education of the council on national defense in Washington. Dr. Musser also presented a paper, "Nephritis," before the county medical society in Montgomery, and spoke on "The Doctor and the Draft" at a meeting of the Fifth District Medical Society, Bastrop.

Dr. Daniel N. Silverman has been named South Regional Committeeman of the American Gastroenterological Association.

Drs. Daniel N. Silverman and Robert A. Katz are the authors of the chapter on "Gastric Analysis" in the Supplement on Biochemistry to Piersol's Cyclopedia of Medicine.

A symposium on complications of pregnancy, including diabetes, tuberculosis and heart disease, was given by the New Orleans Obstetrical and Gynecological Society in the Assembly Hall at Charity Hospital, Thursday, December 19 at 8 p. m.

At a recent staff meeting of the Mercy Hospital Dr. J. K. Howles presented a paper on "Vitamin Therapy in Dermatology"; and Dr. R. H. Bayley discussed "The Uses of the Electrocardiogram."

Dr. Edwin A. Socola spoke on "Preparing a Child for School" in an illustrated lecture sponsored by the Agramonte Premedical Society at Loyola University.

Dr. E. L. King presented a paper on obstetrical hemorrhages and prolonged labor at the Colorado State Medical meeting in Denver, September 14-16. A paper on obstetrical analgesia was also presented by Dr. King before the Texas State Medical Society meeting in Beaumont, November 11.

Dr. Daniel N. Silverman and Robert A. Katz are the editors of a symposium on plasma transfusion, appearing in the International Medical Digest, December and January issues.

Dr. M. Carl Wilensky was re-elected president of the New Orleans Zionist District at a recent meeting of this organization. Dr. Sidney Jacobs was named vice-president.

The Louisiana Association of Public Health Works held its annual meeting at the Jung hotel, December 9-11. Addresses of welcome were made by Drs. John H. Musser and C. Grenes Cole. Dr. George H. Hauser presented a paper on examinations for intestinal parasites at this meeting, and a round-table discussion of virus diseases and rickettsial disorders was led by Dr. John H. Musser and Dr. Roy H. Turner.

At a recent meeting of the Lamar County Medical Society at Meridian the following program was presented by members of this Society: "Management of Acute Spinal Injuries," by Dr. Gilbert C. Anderson; "Analgesia in Obstetrics," by Dr. Arthur Caire, Jr., "Combined Tetanus Diphtheria Immunization," by Dr. Julian Graubarth; and "Treatment of Prolapse of the Uterus," by Dr. Curtis H. Tyrone.

Drs. Alton Ochsner, Ambrose H. Storck and Guy A. Caldwell attended the meeting of the Southern Surgical Association, Hot Springs, December 10-12.

Dr. Alton Ochsner presented a paper on "Thrombophlebitis" before the meeting of the Washington Academy of Surgery, Washington, December 13.

Dr. R. Alec Brown was recently re-elected secretary-treasurer of the Louisiana Association of Public Health Workers.

Dr. Wm. H. Gillentine was recently appointed state health consultant of the National Youth Administration.

HOSPITAL NEWS

The New Orleans Dispensary for Women and Children has moved to its new quarters, 609 Jackson Ave., and can accommodate 50 beds.

The increase in bed space qualifies the dispensary for membership in the American Hospital Association.

The French Hospital has renovated its operating room. Among the new equipment is a Montreid Table; the mechanism can be handled by the anesthetist in adjusting the table to any position desired.

LIBRARIAN'S REPORT

During November, 276 volumes were added to the Library. Of these, 266 were received by binding, 6 by gift and 4 from the New Orleans Medical and Surgical Journal. New titles of recent date are listed below.

The Library has loaned to physicians during the month 1,281 books and journals. An additional 969 volumes have been loaned to students for overnight use, giving a total circulation of 2,250 for November.

Members of the staff have collected material on the following subjects during the month at the request of physicians:

Gastric meals and function tests
Paul Michinard—life and work
Vertigo
Benign tumors in the newborn
Ocular complications of poliomyelitis
Diabetes in pregnancy
Quality point ratio in grading medical students

NEW BOOKS

American Association on Mental Deficiency: Proceedings and Addresses, 1933.

American Therapeutic Society: Transactions, 1940.

Becker, S. W.: Modern Dermatology and Syphilology, 1940.

Manson, Patrick: Tropical Diseases, 1940.

Pelouze, P. S.: Office Urology, 1940.

Rogers, Leonard: Leprosy, 1940.

Southern Surgical Association: Fifty-year Index, 1940.

United States National Institute of Health: National Health Survey, 2v., 1935-36.

Edwin L. Zander M. D., Sec.

LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	

1941 ANNUAL MEETING

The Shreveport Medical Society is actively making plans for the 1941 Annual Meeting to be held in Shreveport, April 21-23, and from all indications a fine meeting is anticipated. You will recall that Shreveport was one of the bright spots of the country during the years of the depression and continues to be a town to be remembered. There appears to be every prospect that the Louisiana State Medical Society meeting in 1941 will be bigger and better, more interesting and more enjoyable than any held here in the past. All of our committees are enthusiastic and looking forward to a highly successful meeting.

The Committee on Commercial Exhibits is apparently going to have enough exhibits to take care of whatever financial needs we may have, when added to the amount allowed by the State Society for expense of the convention.

The Chairman of the Committee on Scientific Exhibits reports that he has sent out applications for exhibit space to prospective exhibitors. All members who desire to exhibit should send information concerning their exhibit to Dr. W. R. Mathews, chairman of this committee.

We feel very fortunate in securing every cooperation from the Washington-Youree Hotel, headquarters for the meeting. The Chairman of the Committee on Hotels, Dr. C. R. Gowen, will be glad to make reservations at the hotel for members of the Society if they will communicate with him.

Below is listed personnel of the various committees on arrangement for the meeting.

General Chairman—Dr. R. T. Lucas.

Advisory Committee—Dr. J. M. Gorton, Chairman; Drs. W. H. Browning, C. B. Erickson, B. C. Garrett, A. A. Herold, J. E. Knighton, W. P. Taylor, and T. B. Tooke.

Banquet and Luncheons—Dr. J. R. Stamper, Chairman; Drs. R. B. DeLee, and C. H. Webb.

Commercial Exhibits—Dr. H. J. Quinn, Chairman; Drs. J. B. Birdwell, and W. J. Norfleet.

Entertainment—Dr. S. G. Wolfe, Chairman; Drs. J. R. Brown, and J. V. Hendrick.

Finance—Dr. D. R. McIntyre, Chairman; Drs. Dorf Bean, and W. R. Harwell.

Golf—Dr. C. P. Rutledge, Chairman; Drs. W. B. Heidorn, and I. B. Rougon.

Halls and Meeting Places—Dr. P. D. Abramson, Chairman; Drs. P. R. Gilmer, and J. E. Heard.

Hotel Reservations and Reception—Dr. C. R. Gowen, Chairman; Drs. W. H. Browning, A. P. Crain, B. C. Garrett, John Hendrick, A. A. Herold, and W. S. Kerlin.

Publicity—Dr. J. M. Bodenheimer, Chairman; Drs. S. W. Boyce, and M. D. Hargrove.

Registration, Signs and Badges—Dr. W. R. Harwell, Chairman; Drs. L. F. Gray, O. C. Rigby, and J. A. Wilkinson.

Scientific Exhibits—Dr. W. R. Mathews, Chairman; Drs. R. H. Riggs, and P. W. Winder.

Woman's Auxiliary—Mrs. J. E. Heard.

THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, MARCH 3-6, 1941

In the January issue of the Journal it was mentioned that among the eighteen outstanding guest speakers who would take part in the program were Drs. Paul Dudley White, Paul A. O'Leary, Owen H. Wangensteen, Ernest E. Irons, Maurice C. Pincoffs, Charles F. McKhann and Cecil S. O'Brien.

All of the speakers are equally well known and prominent in medical circles. Dr. Richard W. TeLinde, speaker in gynecology, is Professor of Gynecology at the Johns Hopkins University and Chief Gynecologist of the Johns Hopkins Hospital. Dr. Louis E. Phaneuf, Professor of Obstetrics and Gynecology at Tufts College Medical School will give four talks during the meeting and will also have three outstanding motion pictures scheduled on the program.

The Section on Pathology is very fortunate in having Dr. Lawrence W. Smith as their guest. Dr. Smith is Professor of Pathology at Temple University School of Medicine, and Pathologist and Director of Laboratories, Temple University Hospital. He is greatly interested, and has done outstanding work, in the treatment of cancer with low temperatures. The topics of Dr. Smith's talks will be, "Reduced Temperature 'Refrigeration' as an Adjunct to the Treatment of Malignant Disease" and "Observations on the Physiologic Mechanism during Generalized 'Refrigeration'." In addition to these lectures he will conduct a Clinico-pathologic Conference with Dr. Frederick A. Coller. Dr. Coller is Professor of Surgery and Chairman of the Department of Surgery at the University of Michigan Medical School.

Dr. W. Wallace Morrison, Clinical Professor of Otolaryngology and Chief of Clinic at the New York Polyclinic Medical School and Hospital, will talk on subjects of interest to the general practitioner as well as to the men specializing in otolaryngology. Dr. George F. Cahill, guest urologist, has selected for his subject, "The Present Urological Conception of Nonspecific Urinary Infections" and "Adrenal Cortical Tumors: Their Types, Diagnosis and Therapy." The Section on Radiology will have for their guest Dr. Leo G. Rigler, Professor and Head of the Department of Radiology and Physical Therapy. Dr. Rigler is the author of articles on roentgen diagnosis and of the textbook "Outline of Roentgen Diagnosis." Dr. Eugene L. Bishop, Director of the Health Program of the Tennessee Valley Authority, will show an interesting motion picture on "Coordination of Malaria Studies and Control on Impounded Waters" followed by an address on the same subject.

The other speakers are Dr. Arthur H. Ruggles, Superintendent of the Butler Hospital and Lecturer in Psychiatry at Yale University School of Medicine and Brown University Medical Department; Dr. George E. Binkley, attending Surgeon in Charge of the Rectal and Colon Department, Memorial Hospital for the Treatment of Cancer and Allied Diseases, and Instructor of Medicine, Cornell University Medical College; and Dr. Paul C. Colonna, Professor of Orthopedic Surgery, University of Oklahoma School of Medicine.

It will be seen from the list of speakers that the Assembly will be of great interest to both specialists and general practitioners. The registration fee of ten dollars covers all features, including four daily round-table luncheons and a smoker.

BIENVILLE PARISH MEDICAL SOCIETY

Drs. S. S. Speer, F. F. Wimberly and V. W. Fletcher were hosts for a meeting at Ringgold, December 17, of the doctors of Bienville Parish. The meeting was held in the dining room of the Allum home, where supper was served.

Dr. M. D. Hargrove, of Shreveport, Councilor of the Fourth District, served as chairman until officers were elected in the reorganization of the Bienville Parish Medical Society.

Dr. Edwin L. Zander, of New Orleans, spoke on "Office Gynecology"; Dr. D. N. Silverman, of New Orleans, spoke on "Common Errors in Gastric Diagnosis"; Drs. P. T. Talbot, A. Penn Crain, and A. Penn Crain, Jr., were also guests on this occasion.

The officers elected for the coming year were Dr. S. S. Speer, of Ringgold, president; Dr. C. L. Langford, of Gibsland, vice-president; Dr. V. W. Fletcher, of Ringgold, secretary-treasurer. Dr. Fletcher was also chosen delegate to the State Society meeting.

V. W. Fletcher, M. D., Sec.

NEW OFFICERS
1941

JACKSON-LINCOLN-UNION

President: Dr. Ragan Green, Ruston
Vice-President: Dr. S. L. White, Ruston
Secretary-Treasurer: Dr. J. J. Bennett, Ruston

POINTE COUPEE PARISH

President: Dr. J. W. Plauche, Morganza
Vice-President: Dr. J. M. Mosely, Lakeland
Secretary-Treasurer: Dr. R. A. Kelly, New Roads

WEBSTER PARISH

President: Dr. Rupert Butler, Springhill
Vice-President: Dr. R. E. Smith, Minden
Secretary-Treasure:r Dr. B. A. Norman, Cotton Valley

LAFAYETTE PARISH

President: Dr. E. E. Guilbeau, Carencro
Vice-President: Dr. L. A. Prejean, Scott
Secretary-Treasurer: Dr. Henry Voorhies, Lafayette

MOREHOUSE PARISH

President: Dr. W. V. Garnier, Bastrop
Vice-President: Dr. J. L. Rawls, Bastrop
Secretary-Treasurer: Dr. F. B. Ogden, Bastrop

IBERIA PARISH

President: Dr. J. D. Martin, New Iberia
Vice-President: Dr. H. M. Flory, New Iberia
Secretary-Treasurer: Dr. C. L. Mengis, New Iberia.

AVOYELLES PARISH

President: Dr. H. J. Kaufman, Jr., Cottonport
Vice-President: Dr. W. F. Couvillion, Marksville
Secretary-Treasurer: Dr. K. A. Roy, Mansura

TANGIPAHOA PARISH

President: Dr. J. DeL. Thames, Hammond
Vice-President: Dr. R. G. Korniker, Ponchatoula
Secretary-Treasurer: Dr. S. J. Cali, Hammond.

NEWS ITEMS

Dr. Herald R. Cox, Principal Bacteriologist of the United States Public Health Service, stationed at the Public Health Service Rocky Mountain Laboratory, Hamilton, Montana, has been unanimously nominated by The Theobald Smith Award Committee to receive the 1940 Theobald Smith award in medical science. This honor is conferred on Doctor Cox for his outstanding research in the rickettsial diseases, resulting in the development of a new technic for the preparation of protective vaccines against Rocky Mountain spotted fever and typhus fever. The presentation was made at the meeting of the American Association for the Advancement of Science held in Philadelphia during December 1940 and January 1941.

The American Association for the Study of Goiter again offers the Van Meter Prize Award of Three Hundred Dollars and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The Award will be made at the annual meeting of the Association which will be held at Boston, Massachusetts, May 26-28, providing essays of sufficient merit are presented in competition.

Dr. Ambrose H. Storck attended the recent meeting of the Southern Surgical Association at Hot Springs, Va., and presented a paper on "Abdominal Injuries."

Assistant Surgeon Ralph W. Pagel has been relieved of duty at Galveston, Texas, and ordered to proceed to the U. S. Marine Hospital, New Orleans.

Passed Assistant Surgeon Joseph Pasternack has been relieved at New Orleans, and ordered to proceed to the U. S. Marine Hospital, Staten Island, New York, for duty.

There is a physician needed for one year at Sunset, Louisiana. Those interested should communicate with Dr. J. L. Prejean or Mr. Paul A. Bechet, of Sunset.

The International College of Surgeons will hold its Fifth International Assembly in Mexico City, August 10-14, 1941, in response to the invitation of the Mexican Government. With the assembly will be scientific exhibits of the latest advances in surgery and commercial demonstrations of the newest equipment.

The general oral and pathologic examinations of the American Board of Obstetrics and Gynecology for all candidates (Groups A and B) will be conducted at Cleveland, Ohio, by the entire Board from Wednesday, May 28, to Monday, June 2, 1941, inclusive, prior to the opening of the annual meeting of the American Medical Association in Cleveland, Ohio.

THE POST GRADUATE SURGICAL ASSEMBLY

The twelfth annual meeting of the Post Graduate Surgical Assembly and the Southeastern Surgical Congress will be held in Richmond, Virginia, March 10-12, 1941. A splendid list of speakers have accepted invitations to address the Assembly. A few of the names that are outstanding include Dr. Irvin Abell and Dr. Fred W. Rankin of Kentucky; Dr. Temple S. Fay of Philadelphia; Dr. Charles F. Geschickter of Baltimore; Dr. Frank H. Lahey of Boston and many others. The Louisiana men who are represented on the provisional program include Dr. Conrad G. Collins and Dr. Alfred B. Longacre. From Mississippi will come Dr. Harley R. Shands of Jackson and Dr. M. M. Snelling of Gulfport.

For further information, those interested should address Dr. B. T. Beasley, Secretary-Treasurer, 701 Hurt Building, Atlanta, Georgia.

The Executive Board of the American Public Health Association announces the dates of the seventieth annual meeting as October 14-17, 1941. The meeting place is Atlantic City, New Jersey. Headquarters for the meeting will be the Convention Hall. Residence headquarters will be the Hotel Traymore.

INFECTIOUS DISEASES IN LOUISIANA

The morbidity report of the Bureau of Epidemiology of the Louisiana State Board of Health for the week ending December 14 showed the first large influx of influenza cases; for this particular week there appeared 321 cases. Other diseases reported in number greater than ten were syphilis 274, gonorrhea 34, tuberculosis 29, cancer 25, pneumonia 22 and diphtheria 11. This week there was one patient with typhus fever in Caddo Parish and one in Orleans Parish. For the week closing December 21, the number of influenza cases had risen to such a great height that apparently the Bureau of Epidemiology had to figure in round numbers because there was the greatest number of cases listed that has ever been listed for any one disease since these reports began to appear in the Journal; 8,000 cases were reported. Following in order of frequency were syphilis with 142 cases, pneumonia 58, gonorrhea 32, cancer 30, hookworm infestation 25, typhoid fever 16 and malaria 14. Three patients with poliomyelitis were discovered this week; one from East Baton Rouge Parish, one from Iberville and one from Orleans. The week which terminated December 28 still showed a large number of cases of influenza, 6,101 being reported. This was followed by syphilis 196, hookworm 52, pneumonia 49, gonorrhea 20 and cancer 17. Except for one case of typhus fever in Orleans Parish, no unusual diseases were reported. The actual number of cases of influenza was materially diminished the first week of January, with 3,235 cases reported, followed by syphilis 117, pneumonia 59, gonorrhea 40, tuberculosis 16, cancer 14 and typhoid fever 12. The incidence of pneumonia came close to the five year average. There was an increase in cases of influenza the week ending January 11; 4,983 being reported, followed by syphilis 177, pneumonia 44, gonorrhea 32, pulmonary tuberculosis 21 and cancer 14. One case of typhus fever was found in Calcasieu Parish.

HEALTH OF NEW ORLEANS

The Bureau of the Census, U. S. Department of Commerce, reports that for the week which ended December 14 there were 138 deaths in the City of New Orleans, divided 81 white and 57 negro, with 18 of these deaths occurring in children under one year of age. These figures compare very closely with the figures of the previous week. For the week which was completed December 21, there were only 130 deaths reported as contrasted with the three year average for the corresponding week, which was 170. Seventy-three of the citizens of New Orleans who died this week were white and 57 negroes and 23 were under one year of age. There was a slight increase in the number of deaths for the week ending December 28. Of the 155 deaths which occurred this week, 105 were in the white population and 50 in the negro. This is a considerably smaller number of deaths in the negro population than usually occurs. Thirteen of the recorded deaths were infants under one year, divided seven white and six colored. The rather sharp increase in the number of deaths in New Orleans the week ending January 4 might reflect in part from the very high incidence of influenza in the city at this time. There were 193 people who died in New Orleans, divided 126 white, 67 negro, with 23 infant deaths.

WOMAN'S AUXILIARY

Louisiana State Medical Society

President—Mrs. Roy Carl Young, Covington.

President-elect—Mrs. Aynaud Hébert, New Orleans.

First Vice-president—Mrs. Joseph E. Heard, Shreveport.

Second Vice-president—Mrs. W. A. Ellender, Houma.

Third Vice-president—Mrs. M. H. Foster, Alexandria.

Fourth Vice-president—Mrs. C. P. Gray, Monroe.

Treasurer—Mrs. M. C. Wiginton, Hammond.

Recording Secretary—Mrs. P. A. Donaldson, Reserve.

Corresponding Secretary—Mrs. Herbert Cannon, Covington.

OUACHITA PARISH

The Woman's Auxiliary to the Ouachita Parish Medical Society held its monthly meeting on October 10, at the Lotus Club, with Mrs. A. D. Tisdale presiding.

The hostesses at this time were Mesdames W. L. Smith, C. P. Gray, Sr., H. V. Collins, and A. L. Peters.

After the roll call and the reading of the minutes, Mrs. O'Donnell, as Chairman of the *Hygeia* Committee, called on Mrs. Perot, Mrs. Peters, and Mrs. McHenry to read papers explaining all about *Hygeia*. The names of the members subscribing to *Hygeia* were read and all members were urged to subscribe if possible and to help get other subscriptions.

Mrs. McHenry read a card calling the attention of the auxiliary to the radio program sponsored by the American Medical Association called "Doc-

tors at Work," on the air every Wednesday evening at 10:30 E. S. T. over NBC. This program will last from November 13, 1940 to June 4, 1941.

The monthly luncheon and business meeting was held at the Lotus Club on November 14. Hostesses on this occasion were Mesdames Pracher, Holloman, Talbot, and Frost.

Mrs. A. D. Tisdale presided over the meeting and read the "Ten Commandments for a Doctor's Wife."

After the reports of the committees, Mrs. Clifford Johnson gave a most interesting review of, "Dynasty of Doctors."

Mrs. Elizabeth Wright, President of Woman's Auxiliary of St. Petersburg, Fla., was our guest at this meeting.

The December luncheon and business meeting was held on Thursday, the twelfth, at the Lotus Club with Mesdames A. G. McHenry, Leon Titche, D. I. Hirsch, Glen Gallaspy, and F. J. Willey as hostesses.

Mrs. A. D. Tisdale presided over the meeting and our honored guests were Mrs. Roy Carl Young of Covington, President of the Woman's Auxiliary to the Louisiana State Medical Society, and her sister, Mrs. C. T. Law, of Shreveport.

After reports from the officers and chairmen of committees, Mrs. Young spoke to us on the aims and activities of the auxiliary, which speech was followed by a round-table discussion.

The luncheon table was beautifully decorated with autumn leaves and flowers. The center piece was a large basket lined with autumn leaves and filled with fruit.

MRS. C. B. FLINN,
Publicity Secretary.

CADDO PARISH

The November meeting of the Shreveport Medical Auxiliary was held at the Department Club.

After a brief business meeting, presided over by the president, Mrs. C. B. Erickson, a most interesting program was presented. Dr. George Wolfe and Miss Sonya Mattus were the guest speakers for the afternoon. Dr. Wolfe spoke on "Infantile Paralysis," in which he discussed the history, pathology, symptoms, treatment and other facts concerning the disease. Miss Mattus gave an informative talk on "Books for Children."

The tea table, presided over by Mrs. L. H. Pirkle and Mrs. I. F. Hawkins, was centered with a lovely arrangement of fruit, around which four cornucopias filled with bronze, yellow and red chrysanthemums were placed. Other seasonal flowers throughout the reception rooms carried out the Thanksgiving and autumn setting.

ST. LANDRY PARISH

The annual card party given by the Woman's Auxiliary was held on October 25 at the Community Center in Opelousas for the benefit of the anti-tuberculosis fund of the St. Landry Parish Medical Society. Fifty beautiful prizes were donated by business firms of Opelousas. Contract and auction bridge, five hundred and poker tables claimed the guests, with a prize awarded at each table; the net proceeds of the evening were ninety-five dollars.

The Committee on Arrangements for the party included Mesdames G. D. Rackley, S. J. Rozas, E. J. Petitjean, L. Lazaro, Gerald Bertinot, and J. L. Prejean. Mrs. F. C. Shute is president of the auxiliary.

RAPIDES PARISH

The Woman's Auxiliary to the Rapides Parish Medical Society held its first meeting of the season on Friday morning, October 11, 1940, at the home of Mrs. J. A. White, Sr., 1740 Jackson Street, Alexandria, with Mrs. J. A. White, Jr. as cohostess.

In the absence of the president the meeting was presided over by Mrs. Earl K. Jones, first vice-president. Mrs. H. O. Barker, one of our past presidents, was the speaker and made a very interesting talk on "Preparedness from a Medical Standpoint."

Aims and projects were discussed including *Hygeia* and work for the Red Cross, which latter was adopted as a project for this year. Auxiliary members will work for the Red Cross in the way of making surgical dressings and garments, knitting and other activities.

One new member, Mrs. Geza Aczel, was introduced.

MRS. WM. J. REIN,
Publicity Chairman.

Respectfully submitted,
MRS. JONAS W. ROSENTHAL,
Press and Publicity Chairman.

BOOK REVIEWS

Savill's System of Clinical Medicine: Edited By Agnes Savill, M. D., and E. C. Warner, M. D., F. R. C. P. Baltimore, William Wood & Co., 1939. Pp. 1141. Price $9.00.

This eleventh edition is a thorough revision of a book that has been found invaluable to students and practitioners of medicine for over thirty years. It is an attempt to approach medicine from the clinical side, and, consequently, the plan of the book is to trace "from effect (symptoms) to cause (the morbid cause) in operation." General principles underlying methods in diagnosis, prognosis and treat-

ment are discussed. The physiognomy of disease is noted and the symptoms and signs arising in the organs and regions of the body and extremities are considered. The diseases arising from the symptoms and signs observed are dealt with clearly and fully. The book is well written and the illustrations are many and good. It is a fine reference work.

I. L. ROBBINS, M. D.

Clinical Diabetes Mellitus and Hyperinsulinism: By Russell Wilder, M. D., Ph. D., F. A. C. P. Philadelphia, W. B. Saunders Co., 1940. Pp. 459. Price $6.00.

The book is divided into two parts. The first and greater part deals with diabetes mellitus. The author places greater emphasis on the clinical aspect of this illness and considers in detail diagnosis, treatment, and the care of complications. Most of the commonly associated diseases, such as hemochromatosis, diseases of the thyroid gland complicating diabetes, diseases of other endocrine glands complicating diabetes, as well as arteriosclerosis and diseases of the heart, are fully described. One chapter is devoted to diabetes in pregnancy and another to surgical operations in diabetes, two conditions which put to the highest test our knowledge of diabetic management. The practicability of the volume is enhanced by the inclusion of diabetic diets and tables of food values.

The last section of the book is concerned with hyperinsulinism. Diagnostic criteria are enumerated, treatment both medical and surgical is discussed and evaluated. Individual case reports are included so that the reader may more fully appreciate the clinical picture.

The book is good reading, valuable as a reference, and a worth-while addition to any practitioner's library.

NORTON VOORHIES, M. D.

Handbook of Hearing Aids: By A. F. Niemoeller, A. B., M. A., B. S.; foreword by Harold Hays, M. D., F. A. C. S. New York, Harvest House, 1940. Pp. 156. Price $3.00.

This book gives a short description of practically all of the modern electrical hearing aids, both vacuum tube and carbon types. There are useful chapters on the care of hearing aid batteries, how to test hearing aids, and how to use hearing aids. Also there is a chapter on how to buy hearing aids which should be very helpful to the hearing aid purchaser, but probably not to the liking of some of the high pressure salesmen that we see today.

The book is recommended for study to both otologists and the deafened individual contemplating purchasing a hearing aid.

H. L. KEARNEY, M. D.

The Chinese Way in Medicine: By Edward H. Hume. Baltimore, Johns Hopkins Press, 1940. Por; pp. 189. Price $2.25.

This is another volume in the excellent series of the Hideyo Noguchi Lectures. In its 189 pages only a brief glimpse of the enormous expanse of Chinese medical history can be presented, but this glimpse is sufficient clearly to reveal the predominant influence of tradition on current medical practice. We are shown not only what the Chinese practice in medicine but why they do so.

In Lecture I (The Universe and Man in Chinese Medicine), Dr. Hume dilates upon the Chinese attitude toward life, death, health and disease. All life, animal, vegetable, and human, is part of a totality in which disease and death are simply normal components. The individual's quest for health is to be achieved by bringing his spiritual and bodily being into harmony with all the forces of the universe.

In Lecture II (The Founders and Chief Exemplars of Chinese Medicine), Dr. Hume draws attention to a few of the illustrious medical personalities of past centuries, whose names and deeds are widely known throughout China today, not only by scholars and physicians, but workmen and farmers.

In Lecture III (Some Distinctive Contributions of Chinese Medicine), we discover that the Chinese early established medical libraries and wrote exhaustively upon such topics as leprosy, venereal disease, smallpox, typhoid, beriberi, gynecology, and ophthalmology. Medicaments reached amazing development; among those herbals and minerals still in use and of permanent value are stramonium, ephedrine, iodine, chaulmoogra oil, and arsenic. Observation and inquiry were emphasized three thousand years before Sydenham. Acupuncture was stressed, while the doctrine of the pulse was so elaborated that nearly the whole system of medicine centered around it.

Although Chinese medicine was predominantly philosophic in conception, there did evolve procedures of real and permanent value for both diagnosis and treatment. These three lectures showing the way thereof form an edifying and interesting book.

R. S. MUNGER, M. D.

The Foot and Ankle, Their Injuries, Diseases, Deformities and Disabilities: By Philip Lewin, M. D., F. A. C. S. Philadelphia, Lea & Febiger, 1940. Pp. 620. Price $9.00.

This new book on the foot and ankle is a timely one, inasmuch as it is the only one of the several recently published which attempts to cover all the problems of the lower extremity from an orthopedic viewpoint, and still retains enough simplicity to be used as a guide to diagnosis and treatment by the average man, who possesses no special knowledge or training along orthopedic lines.

The basic anatomy, physiology and mechanics of the foot and ankle are well described, and the application of these basic principles of function is made throughout the book. The major portion of the volume concerns itself with a discussion of almost every conceivable disturbance which might be encountered in the region of the foot and ankle. The extensive character of the subject matter taken up alone makes the book invaluable for any student of orthopedics, and of extreme value as a reference book for anyone who must see and treat the foot and ankle in his office practice occasionally.

The treatment of the various disorders is discussed under each chapter and subdivision heading, making for simplicity in locating a single subject. The chief criticism of the book, however, can be directed toward this same phase. In describing operative procedures or conservative methods of treatment, too often a large group of opinions and procedures will be presented, but no attempt is made to evaluate them, or to aid the reader in judging just which of the various methods offered he should try in any given case. True, to the man who is interested, it offers a quick, accurate and concise resumé of the information available today, and the excellent bibliography can be used for further study if desired.

The book is well written, readable and accurate in its information, and furnishes a better reference on the foot and ankle in the reviewer's opinion than any other book published to date.

FRANK J. COX, M. D.

PUBLICATIONS RECEIVED

The Blakiston Company, Philadelphia: Recent Advances in Endocrinology, by A T. Cameron, M. A., D. Sc. (Edin.), F. I. C., F. R. C. S. The Anatomy of the Eye and Orbit, by Eugene Wolff, M. B., B. S. (Lond.), F. R. C. S. (Eng.).

The Brown-White Company, Kansas City, Mo.; Poems of a Doctor, by Edward Lovelle Stewart, M. D.

The Commonwealth Fund, New York City: Ways to Community Health Education, by Ira V. Hiscock, with the collaboration of Mary P. Connolly, Marjorie Delavan, Raymond S. Patterson, and William H. F. Warthen. Rheumatic Fever, by May G. Wilson, M. D. Mosquito Control, by William B. Herms, Sc. D., and Harold F. Gray, Gr. P. H. Insulin, Its Chemistry and Physiology, by Hans F. Jensen, Ph. D.

Doubleday, Doran and Company, Inc., New York City: Strange Malady, the Story of Allergy, by Warren T. Vaughn, M. D.

Froben Press, New York City: The Emperor's Itch, by Reuben Friedman, M. D.

Funk & Wagnalls Company, New York City: Growing Out of Babyhood, by Williams S. Sadler, M. D., F. A. P. A., and Lena K. Sadler, M. D., F. A. C. S.

Harvard University Press, Cambridge, Mass.: The Endocrine Function of Iodine, by William Thomas Salter.

The Macmillan Company, New York City: Berkeley Moynihan, Surgeon, by Donald Bateman. The Neuroses in War, by several authors under the editorship of Emanuel Miller, M. A. (Cantab.), M. R. C. P., D. P. M. (Cambs), with a concluding chapter by H. Crichton-Miller, M. D., F. R. C. P.

C. V. Mosby Company, St. Louis: Clinical Pellagra, by Seale Harris, M. D., assisted by Seale Harris, Jr., M. D.

Oxford University Press, New York City: Carlos Finlay and Yellow Fever, by Carlos E. Finlay, M. D., F. A. C. S., edited by Morton C. Kahn, M. A., Ph. D., Sc. D.

Charles C. Thomas, Springfield, Illinois: The Medical Reports of John Y. Bassett, M. D., the Alabama Student, with an introduction by Daniel C. Elkin, M. D. The Role of the Liver in Surgery, by Frederick Fitzherbert Boyce, B. S., M. D.

The Williams & Wilkins Company, Baltimore: A Guide to Human Parasitology, by D. B. Blacklock, M. D. (Edin.), D. P. H. (London); D. T. M. (Liver.), and T. Southwell, D. Sc., Ph. D., A. R. C. Sc., F. Z. S., F. R. S. E.

The John C. Winston Company, Philadelphia: Test Tubes and Dragon Scales, by George C. Basil, M. D.

The Year Book Publishers, Inc., Chicago: The 1940 Year Book of Industrial and Orthopedic Surgery, edited by Charles F. Painter, M. D. The 1940 Year Book of Pathology and Immunology, edited by Howard T. Karsner, M. D., and Sanford B. Hooker, A. M., M. D.